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ORIGINAL RESEARCH

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Bariatric surgery for Prader-Willi syndrome was ineffective in producing sustainable weight loss: Long term results for up to 10 years

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Summary

Background: Obesity control in Prader-Willi syndrome (PWS) is notoriously difficult. The role of bariatric surgery in PWS remains controversial as long-term data are lacking.

Objectives: To evaluate the 10-year outcomes of bariatric surgery in PWS.

Methods: This was a prospective observational study on PWS patients who received bariatric surgery and multidisciplinary follow-up programmes for obesity control. Outcomes on weight reduction and comorbidity resolution were evaluated.

Results: Between 2008 and 2013, five PWS patients (two males, mean age 19.2 ± 3.0 years) with body mass index of 47.3 ± 6.9 kg m^{-2} received sleeve gastrectomy (n = 2), one anastomosis gastric bypass (n = 2), and Roux-en-Y gastric bypass (n = 1) after failing all non-operative weight loss programmes. The median follow-up was 8.4 ± 2.2 years. The best mean percentage of total weight loss (%TWL) was achieved at 2 years (24.7%). %TWL dropped to 23.3% at 3 years, 11.9% at 5 years, 4.1% at 8 years, and 0% at 10 years. Each patient had at least three comorbidities preoperatively, but none of them had resolution of any one of the comorbidities at the last follow-up.

Conclusions: Bariatric surgery could not produce sustainable long-term weight loss or comorbidity resolution in PWS. This study suggests that bariatric surgery cannot be recommended to PWS patients as a standard treatment.

KEYWORDS

bariatric surgery, morbid, obesity, paediatric obesity, Prader-Willi syndrome, weight loss

1 | INTRODUCTION

Prader-Willi syndrome (PWS) is a complex genetic disorder caused by genomic imprinting errors on chromosome 15.[1,2] It is a multisystem condition characterized by mental retardation, hypogonadotropic hypogonadism, growth failure, and other endocrine disturbances.[3,4] Compulsive hyperphagia and progressive weight gain are the most prominent phenotypic manifestations that can invariably lead to severe obesity in the early childhood. The development of uncontrolled obesity and obesity-related comorbidities often results in premature death at young age.[5] Control of obesity is critically important in the overall management of PWS.

The use of bariatric surgery to treat morbid obesity in PWS remains controversial.[6,7] In the nonsyndromic adult population,

bariatric surgery has been clearly established as a highly effective intervention in managing morbid obesity and its related comorbidities.[8,9] To treat nonsyndromic childhood and adolescent obesity, bariatric surgery has been increasingly advocated due to its favourable weight loss outcomes similar to adults.[10] As for PWS, while the contemporary bariatric operations are regarded as safe procedures, the efficacy of bariatric surgery on weight loss and comorbidity resolution was largely inconsistent.[11-33] Long-term follow-up data were particularly lacking.[30] Because of the intrinsic problem of compulsive hyperphagia, the long-term sustainability of the surgical weight loss effect remains the most critical issue in evaluating the role of bariatric surgery in PWS. The objective of the present study was to evaluate the 10-year experiences of bariatric surgery on PWS patients.

2 | METHODS

This was a prospective observational study on consecutive patients with PWS who received laparoscopic sleeve gastrectomy (LSG), laparoscopic one anastomosis gastric bypass (OAGB), and laparoscopic Roux-en-Y gastric bypass (RYGB) in our unit. All patients had fulfilled the clinical and genetic manifestations of the revised Holm et al criteria for the diagnosis of PWS.[7,34,35] They were referred to our clinic for the management of morbid obesity by the paediatric endocrinologists after failing all non-surgical weight reduction programmes. Upon referral to our clinic, a multidisciplinary bariatric surgery counselling programme was provided to all patients and their caregivers for at least 6 months. They were periodically reviewed by a designated bariatric surgeon for counselling on the risks of bariatric surgery, the need of dietary commitments, and the importance of behavioural modifications. Regular dietary and behavioural educations were also provided by designated dietitians and bariatric nurses. Anaesthetic assessment was routinely conducted.

2.1 | Patients

Upon completion of the counselling programme, patients were considered eligible for bariatric surgery when (a) they had a body mass index (BMI) $\geq$ 35 kg m^{-2} or BMI $\geq$ 30 kg m^{-2} with at least two comorbid conditions or BMI > 99th percentile for their age[36]; (b) they had a dedicated caregiver from their families; (c) both the patients and their caregivers had understood and accepted the risks of bariatric surgery; and (d) the contraindications for surgery were absent. We excluded patients who had previous gastric or intestinal surgery or had hormonal disturbances other than those associated with PWS (such as hypothyroidism or adrenal gland dysfunction). The study protocol was approved by our institutional ethics review board and was conducted in accordance with the ethical standards of the Helsinki Declaration of 1975. Written informed consent was obtained from all patients and their caregivers for study recruitment.

2.2 | Selection of operation type

The choice of LSG, OAGB, and RYGB were explained to each patient and their caregivers in details by the bariatric surgeons. The risks and benefits of each procedure type were explained and compared. Written information about each procedure type was also provided. For patients with metabolic syndrome, they were counselled for either OAGB or RYGB for better control of their metabolic diseases. For those without metabolic syndrome, LSG was alternatively suggested for lower operative complexity and complication profiles. The final decision on the type of surgery was jointly made by the patients, their caregivers, and the bariatric surgeons.

2.3 | Surgical technique

All procedures were performed by a single surgeon. Our operative techniques of LSG and OAGB had been previously described.[32,37] For all cases of LSG and OAGB, a 40Fr intragastric bougie was used for size calibration of the gastric pouch. For RYGB, a gastric pouch was created using a linear stapler with size calibration by a 40Fr intragastric bougie. Standardized lengths of 100-cm biliopancreatic limb and 100-cm Roux limb were chosen. Antecolic Roux-en-Y gastrojejunal and jejuno-jejunal anastomoses were constructed using linear staplers.

2.4 | Follow-up assessment

All patients were prospectively followed at 1, 3, 6, and 12 months and then annually in an outpatient basis. To ensure compliance to follow-up, repeated telephone calls were given to those who did not turn up for follow-up until they reattended the clinic. To minimize the problem of nonadherence to instructions, dietary and behavioural educations were given to the patients and their caregivers by designated dietitians and bariatric surgeons at each follow-up visit. Additional clinic reviews were arranged for education reinforcement when weight regain was observed.

2.5 | Outcome measures

The percentage of total weight loss (%TWL) and the percentage of excess weight loss (%EWL) were used to represent the extent of weight reduction. Successful weight loss was defined as having %EWL > 50%. The primary outcome was the long-term changes in weight parameters. The changes in comorbidity status were measured as secondary outcomes. Type 2 diabetes mellitus (T2DM) was defined using the World Health Organization 1999 diagnostic criteria (fasting blood glucose $\geq$ 7.0 mmol L^{-1} or 2-hour postprandial plasma glucose $\geq$ 11.1 mmol L^{-1}).[38] Remission of T2DM was defined using the American Diabetes Association 2009 criteria.[39] Remission of dyslipidaemia was defined as normalized lipid profile (triglycerides < 1.7 mmol L^{-1}, total cholesterol < 5.2 mmol L^{-1}, and LDL cholesterol < 2.6 mmol L^{-1}) without the use of lipid lowering agents for 12 months. Remission

of obstructive sleep apnoea syndrome was defined as complete resolution of snoring during sleep without the use of continuous positive airway pressure (CPAP).

2.6 | Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 24 (IBM, New York, USA). Changes in post-operative weight parameters were compared by the Wilcoxon signed-rank test. Chi-square test or Fisher exact test was used for analysis of nominal and categorical data. A two-sided *P* value of <0.05 was regarded as significant.

3 | RESULTS

Between June 2008 and January 2013, five Chinese PWS patients (two males and three females) with mean age of 19.2 ± 3.0 years (range 15-23) underwent LSG (n = 2), OAGB (n = 2), and RYGB (n = 1) in our unit. Their baseline characteristics are summarized in Table 1. The median follow-up duration was 8.0 ± 2.3 years. All patients had completed more than 5 years of follow-up. There was no lost-to-follow-up in this study. All patients had a genetic subtype of paternal deletion (100%). None of the patients had growth hormone deficiency or had been put on growth hormone replacement before or after the operation.

3.1 | Perioperative data

There was no open conversion in all procedures. The mean operating time was 155.0 ± 72.0 minutes. The mean hospital stay was 8.0 ± 1.6 days. There was no perioperative mortality, complications, or reoperations.

3.2 | Weight control

The 10-year changes in body weight are depicted in Figure 1, and the summative changes in weight parameters are summarized in Table 2. The mean BMI reduced significantly from 47.3 ± 6.9 kg m^{-2} preoperatively to 36.5 ± 5.7 kg m^{-2} at 1 year (*P* = .04) and 35.3 ± 4.8 kg m^{-2} at 2 years (*P* = .04). The nadir body weight was achieved at 2 years with the mean %TWL of 24.7 ± 10.5% and the mean %EWL of 52.7 ± 22.0%. Three out of five patients could achieve successful weight loss (%EWL > 50%) at 2 years.

After the second year, there was progressive weight rebound. The mean BMI increased to 36.0 ± 4.3 kg m^{-2} at 3 years (*P* = .04), 38.9 ± 6.9 kg m^{-2} at 4 years (*P* = .08), 41.6 ± 7.6 kg m^{-2} at 5 years (*P* = .05), and 43.0 ± 7.9 kg m^{-2} at 6 years (*P* = .14). After the sixth year, the mean BMI returned to the baseline BMI and even increased further. The mean BMI was 48.4 ± 8.9 kg m^{-2} at 7 years, 48.0 ± 8.4 kg m^{-2} at 8 years, 48.6 ± 7.6 kg m^{-2} at 9 years, and 50.3 ± 7.7 kg m^{-2} at 10 years. As for the extent of weight loss, there was progressive decrease in %TWL from 2 years onwards. The mean %TWL were 23.3% at 3 years, 17.2% at 4 years, 11.9% at 5 years, 9.2% at 6 years, 3.4% at 7 years, 4.1% at 8 years, and 2.7% at 9 years. At 10 years, the mean %TWL was below 0. None of the patients could achieve successful weight loss from 6 years onwards. Regardless of the procedure type, the trend of weight changes was similar in all patients (Figure 1).

3.3 | Comorbidity change

The changes in obesity-related comorbidities are summarized in Table 3. Before surgery, T2DM was present in two patients (40.0%). One patient (patient 4) had persistent T2DM after OAGB. Despite the initial improvement in insulin dosage for 2 years, her insulin requirement increased progressively from 2 years onwards and returned to her preoperative dose by 5 years. The other T2DM patient (patient 5) developed complete remission after RYGB in the first 2 years but developed recurrence at 4 years and was put back on oral anti-diabetic drugs. The latest HbA1c levels of both patients were similar to their preoperative levels. At baseline, none of the patients had hypertension. Two patients (patients 4 and 5) developed new-onset hypertension at 3 and 5 years, respectively, and were treated with anti-hypertensive medications. Dyslipidaemia was present in all patients but only one of them required lipid-lowering agents before operation. After surgery, none of the patients developed remission of dyslipidaemia throughout the post-operative period. Obstructive sleep apnoea syndrome (OSAS) was present in all five patients, but only three of them were using CPAP at baseline because two patients were intolerant to CPAP. Despite mild improvement in snoring symptoms in all patients in the first 2 years, none of them developed remission of symptoms at the latest follow-up. Three patients had non-alcoholic fatty liver disease preoperatively. There was no significant change in the mean post-operative levels of all liver enzymes throughout the post-operative period (*P* > .05).

During the follow-up period, one patient (patient 4) developed sudden death at post-operative 78 months at the age of 27. She was found arrest during sleep, and the cause of death was suspected to be apnoeic or undiagnosed cardiac events. Post-mortem examination was rejected by her family.

3.4 | Revisional surgery

In response to weight regain or suboptimal weight loss, barium meal studies were performed in patient 1 (at 5 years), patient 2 (at 5 years), patient 3 (at 5 years), and patient 4 (at 4 years). None of these patients had abnormal gastric pouch dilatation demonstrated. Gastrojejunal anastomotic dilatation was not present in patients 2 and 4. Revisional surgery from LSG to malabsorptive procedures was offered to patients 1 and 3 at post-operative 5 years due to weight regain. Revisional surgery to other types of malabsorptive procedures was also offered to patient 2 at post-operative 8 years for weight regain and patient 4 at post-operative 4 years for suboptimal weight loss. However, none of these patients or their caregivers agreed for revisional surgery.

TABLE 1 Baseline characteristics of five patients with Prader-Willi syndrome undergoing bariatric surgery

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	All Patients (n = 5)[a]
Age, y	15	18	23	21	19	19.2 ± 3.0
Gender	M	F	F	F	M	-
Body weight, kg	120.7	102.2	98.3	68.4	93.3	96.6 ± 18.8
Body height, cm	145.0	152.0	143.0	133.5	139.0	142.5 ± 6.9
BMI, kg m^{-2}	57.4	44.2	48.1	38.4	48.3	47.3 ± 6.9
Waist circumference, cm	135.0	117.0	115.0	110.5	121.0	119.7 ± 9.4
Percentage of body fat, %	49.4	64.3	49.3	39.9	57.5	52.1 ± 9.2
Obesity-related comorbidities						
T2DM	No	No	No	Yes	Yes	2 (40.0%)[b]
Prediabetes	No	Yes	No	No	No	1 (20.0%)[b]
Hypertension	No	No	No	No	No	0 (0%)[b]
Dyslipidaemia	Yes	Yes	Yes	Yes	Yes	4 (80.0%)[b]
OSAS	Yes	Yes	Yes	Yes	Yes	5 (100%)[b]
NAFLD	Yes	No	Yes	Yes	No	3 (60.0%)[b]
Osteoarthritis	No	No	No	No	Yes	1 (20.0%)[b]
Use of chronic medications	None	None	Medroxyprogesterone	Insulin, metformin, acarbose, spironolactone, furosemide, valsartan, and medroxyprogesterone	Insulin and testosterone /	
Growth hormone deficiency	No	No	No	No	No	0 (0%)
Use of growth hormone	No	No	No	No	No	0 (0%)
Fasting blood glucose, mmol L^{-1}	5.8	4.4	4.5	9.1	4.7	5.7 ± 2.0
Glycosylated haemoglobin, %	5.0	6.2	5.6	11.3	8.9	7.4 ± 2.6
Total cholesterol, mmol L^{-1}	4.8	4.7	4.2	2.6	5.3	4.3 ± 1.0
Triglycerides, mmol L^{-1}	0.7	2.3	1.3	3.4	1.5	1.8 ± 1.0
LDL cholesterol, mmol L^{-1}	2.9	2.4	2.7	0.4	3.6	2.4 ± 1.2
Type of surgery	LSG	OAGB	LSG	OAGB	RYGB	-
Operative time, min	105	120	85	240	225	155.0 ± 72.0
Hospital stay, d	8	7	6	9	10	8.0 ± 1.6
Follow-up duration, y	10	10	10	6	6	8.4 ± 2.2

Abbreviations: BMI, body mass index; F, female; LDL, low density lipoproteins; LSG, laparoscopic sleeve gastrectomy; M, male; NAFLD, non-alcoholic fatty liver disease; OAGB, laparoscopic one anastomosis gastric bypass; OSAS, obstructive sleep apnoea syndrome; RYGB, laparoscopic Roux-en-Y gastric bypass; T2DM, type 2 diabetes mellitus.

[a]Data are mean ± standard deviation unless stated otherwise.

[b]Data are count (percent).

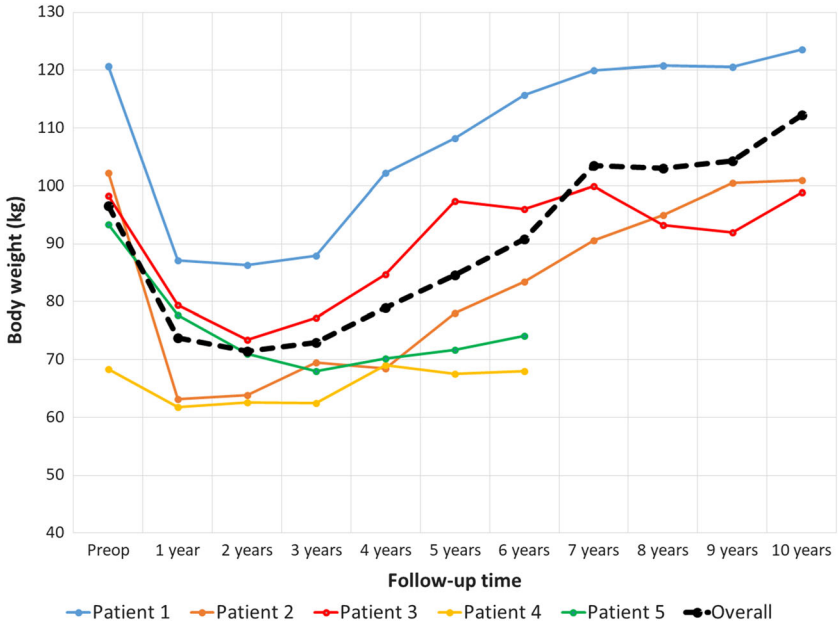

FIGURE 1 Changes in body weight after bariatric surgery in Prader-Willi syndrome patients

4 | DISCUSSION

In this study, bariatric surgery was ineffective in producing sustainable weight loss and comorbidity resolution in PWS patients regardless of the procedure type. Despite an initial success of weight reduction in the first 2 years, almost all patients had returned to their original body weight by 6 years. None of the patients had sustainable comorbidity resolution during long-term follow-up. Obesity-related premature mortality could not be prevented in one of the patients.

Control of obesity in PWS is almost always difficult. Because of uncorrectable compulsive hyperphagia and food craving behaviour, non-operative interventions by behavioural modifications, calorie restriction, and close supervision are often futile.[7] Surgical weight loss by bariatric surgery had been attempted on PWS patients for several decades (Table 4). Majority of the published results were short-term follow-up data of 3 years or less.* Although the reported early %EWL varied from 11.2% to 100.8%, good short-term weight loss results were generally achieved irrespective of the procedure types. In the current study, the best weight loss outcomes were observed at 2 years. These concurred with the literature data that bariatric surgery could produce a good short-term weight loss results in PWS.

The controversy of the use of bariatric surgery in PWS stays at the long-term sustainability of the surgical weight loss effects. As demonstrated in the Swedish Obese Subjects study, the weight loss effects of bariatric surgery in normal adults were sustainable for up to 20 years regardless of the procedure types.[40] In nonsyndromic paediatric populations, recent systematic reviews showed that significant and durable weight loss results could be achieved for up to 7 years.[10] In PWS, our results demonstrated that bariatric surgery had poor weight loss efficacy over time. Similarly, Alqahtani et al reported the 5-year data of the largest literature series of 24 PWS patients receiving vertical sleeve gastrectomy.[30] Their %EWL dropped progressively from the best result of 59.7% at 1 year to 38.4% at 5 years. When compared with the nonsyndromic control subjects, the %EWL of PWS were significantly more inferior. Even with malabsorptive procedures, the weight loss efficacy in PWS was shown to be nonsustainable. Marceau et al reported the remarkable weight regain back to the original weight at 4 to 10 years after duodenal switch (DS) in three PWS patients.[27] Another study on 15 PWS patients undergoing biliopancreatic diversion (BPD) by Marinari et al showed a progressive drop of %EWL over 10 years.[22] Overall, majority of the literature reports and our 10-year data could not achieve a sustainable weight loss efficacy by 5 to 10 years.

Comparing with the other literature data that reported the 5-year outcomes of bariatric surgery on PWS patients, the weight loss outcomes of our patient cohort were slightly more inferior (Table 4). While the weight loss results of the studies by Marceau et al and Marinari et al were representing the outcomes of BPD and DS,[22,27] our data were focusing on LSG and gastric bypass only. Because the weight loss results of BPD and DS were known to be better than LSG and gastric bypass in nonsyndromic adults, we believed that such differences were still present in PWS patients. When compared with the study by Alqahtani et al,[30] the mean age of our patient cohort was much older than their patients (19.2 vs 10.7 years old). While our study was using a BMI value of 25 kg m^{-2} as the ideal body weight to calculate the %EWL, their study was using the 85th percentile weight value for age and gender on the Centers for Disease Control and Prevention growth chart to estimate their %EWL. Hence, direct comparison of the %EWL results of these two studies were bound to be inaccurate. Regardless of these differences, the trend of progressive drop in %EWL over time were consistent in all these three studies and our study.

Comorbidity improvement and resolution after bariatric surgery in PWS was disappointing over time. In contrast to the study by Alqahtani et al that showed a rate of 86% to 100% for comorbidity resolution or improvement, our study did not demonstrate a

*References 11,13,18,21,23-26,28,29.

TABLE 2 Changes in weight parameters after bariatric surgery in patients with Prader-Willi syndrome

		Preoperative (n = 5)	1 y (n = 5)	2 y (n = 5)	3 y (n = 5)	4 y (n = 5)	5 y (n = 5)	6 y (n = 4)	7 y (n = 3)	8 y (n = 3)	9 y (n = 3)	10 y (n = 2)
Body weight, kg	Mean	96.6 ± 18.8	73.8 ± 11.0	71.4 ± 9.5	73.0 ± 9.8	78.9 ± 14.6	84.6 ± 17.5	87.5 ± 19.0	103.5 ± 15.0	103.0 ± 15.4	104.3 ± 14.6	107.8 ± 13.6
	Patient 1	120.7	87.1	86.3	87.9	102.2	108.2	115.7	120.0	120.8	120.5	123.5
	Patient 2	102.2	63.2	63.9	69.5	68.5	78.0	83.5	90.6	95.0	100.5	101.0
	Patient 3	98.3	79.4	73.4	77.2	84.7	97.4	96.0	99.9	93.2	92.0	98.9
	Patient 4	68.4	61.8	62.6	62.5	69.0	67.5	68.0	-	-	-	-
	Patient 5	93.3	77.7	71.0	68.0	70.2	71.7	74.1	-	-	-	-
BMI, kg m^{-2}	Mean	47.3 ± 6.9	36.5 ± 5.7	35.3 ± 4.8	36.0 ± 4.3	38.9 ± 6.9	41.6 ± 7.6	43.0 ± 7.9	48.4 ± 8.9	48.0 ± 8.4	48.6 ± 7.6	50.3 ± 7.7
	Patient 1	57.4	41.4	41.1	41.8	48.6	51.5	55.0	57.1	57.5	57.3	58.7
	Patient 2	44.2	27.4	27.7	30.1	29.7	33.8	36.1	39.2	41.1	43.5	43.7
	Patient 3	48.1	38.8	35.9	37.8	41.4	47.6	47.0	48.9	45.6	45.0	48.4
	Patient 4	38.4	34.7	35.1	35.1	38.7	37.9	38.4	-	-	-	-
	Patient 5	48.3	40.2	36.8	35.2	36.3	37.1	38.4	-	-	-	-
EWL, %	Mean	-	47.9 ± 23.6	52.7 ± 22.0	49.5 ± 17.8	36.1 ± 29.3	25.3 ± 24.6	19.7 ± 20.8	7.9 ± 15.9	9.0 ± 8.3	5.8 ± 6.8	-1.2 ± 3.9
	Patient 1	-	49.3	50.5	48.1	27.2	18.4	7.3	1.0	-0.1	-0.3	-5.1
	Patient 2	-	87.8	86.2	73.6	75.8	54.5	42.1	26.1	16.2	3.8	2.7
	Patient 3	-	40.1	52.8	44.7	28.8	1.9	4.9	-3.4	10.8	13.4	-1.3
	Patient 4	-	27.7	24.3	24.7	-2.5	3.8	1.7	-	-	-	-
	Patient 5	-	34.7	49.6	56.2	51.3	48.0	42.7	-	-	-	-
TWL, %	Mean	-	22.3 ± 11.0	24.7 ± 10.5	23.3 ± 9.0	17.2 ± 12.7	11.9 ± 11.2	9.2 ± 9.5	3.4 ± 6.9	4.1 ± 3.7	2.7 ± 3.3	-0.2 ± 2.3
	Patient 1	-	27.8	28.5	27.2	15.3	10.4	4.1	0.6	-0.1	0.2	-2.3
	Patient 2	-	38.2	37.5	32.0	33.0	23.7	18.3	11.4	7.0	1.7	2.2
	Patient 3	-	19.2	25.3	21.5	13.8	0.9	2.3	-1.6	5.2	6.4	-0.6
	Patient 4	-	9.7	8.5	8.6	-0.9	1.3	0.6	-	-	-	-
	Patient 5	-	16.7	23.9	27.1	24.8	23.2	20.6	-	-	-	-

Note. Data are mean ± standard deviations unless otherwise stated.

Abbreviations: BMI, body-mass-index; EWL, percentage of excess weight loss; TWL, percentage of total weight loss.

TABLE 3 Prevalence of comorbidities before bariatric surgery and at the latest follow-up

		Post-operative			
	Preoperative	Remission	Improvement	No change	Recurrence/new onset
T2DM	2	0	0	1 (50%)	1 (50%)
Prediabetes	1	0	0	1 (100%)	0
Hypertension	0	0	0	0	2 (100%)
Dyslipidaemia	5	0	0	5 (100%)	0
OSAS	5	0	0	5 (100%)	0
NAFLD	4	0	0	4 (100%)	0
Osteoarthritis	1	0	1 (100%)	0	0

Note. Data are count (percent).

Abbreviations: NAFLD, non-alcoholic fatty liver disease; OSAS, obstructive sleep apnoea syndrome; T2DM, type 2 diabetes mellitus.

TABLE 4 Literature results of bariatric surgery on patients with Prader-Willi syndrome

Author	Year	Sample Size	Mean Age, y	Gender (M:F)	Mean BMI, kg m^{-2}	Procedure Type	Complications	FU Duration, mo	Last FU EWL%	3-y EWL%	5-y EWL%	10-y EWL%
Randolph et al[11]	1974	1	11	1:0	46.9	Jejunoileal bypass	None	36	84.0	84.0	NA	NA
Anderson et al[12]	1980	11	NA	7:4	NA	Gastric bypass (10), gastroplasty (1)	Wound infection (1)	NA	NA	-	-	-
Touquet et al[13]	1983	1	24	1:0	71.8	Jejunoileal bypass	Wound infection, deep vein thrombosis, pulmonary embolism	12	100.8	-	-	-
Brossy[14]	1989	1	31	1:0	37.6	BPD	None	NA	NA	-	-	-
Miyata et al[15]												
Laurent-Jaccard et al[16]	1991	3	27.7	2:1	34.5	BPD	Ileus (1), severe diarrhoea (1), anaemia (1)	53-87	3.4-44.4	-	-	-
Dousei et al[17]	1992	1	21	0:1	NA	VBG	None	60	0	-	-	-
Mason et al[18]	1995	1	20	1:0	NA	VBG	None	36	0			
Antal et al[19]	1996	2	17.5	1:1	54.2	BPD	Respiratory (1)	12-24	33.9-89.3	-	-	-
Chelala et al[20]	1997	1	NA	NA	NA	LAGB	Death (1)	NA	NA	-	-	-
Grugni et al[21]	2000	1	21	0:1	50.0	BPD	Ventral hernia	36	11.2			
Marinari et al[22]	2001	15	21	9:6	53.0	BPD	None	102	NA	56	46	40
Kobayashi et al[23]	2003	1	30	1:0	50.0	RYGB	None	4	28.5	-	-	-
De Almeida et al[24]	2005	2	23.5	1:1	58	BPD	None	12-28	48-58	-	-	-
Papavramidis et al[25]	2006	1	20	0:1	74.3	BPD-DS	None	18	61.8	-	-	-
De Peppo et al[26]	2008	12	18.7	4:8	47.9	BIB	Death (1), gastric perforation (1), Balloon rupture	8	24.3	-	-	-

(Continues)

TABLE 4 (Continued)

Author	Year	Sample Size	Mean Age, y	Gender (M:F)	Mean BMI, kg m^{-2}	Procedure Type	Complications	FU Duration, mo	Last FU EWL%	3-y EWL%	5-y EWL%	10-y EWL%
							(1), diarrhoea (1), gastric bezoar (2)					
Marceau et al[27]	2010	3	15.7	2:1	61.6	DS	Death (1), septicaemia (1), adrenal insufficiency (1), prolonged intubation (2), high fever (1), revisional surgery (2)	48-168	0-65.2	-	-	-
Yu et al[28]	2013	1	17	0:1	46.7	LSG	None	14	45.8	-	-	-
Musella et al[29]	2014	3	15.6	3:0	51.0	OAGB-MGB	None	14	62-79	-	-	-
Alqahtani et al[30]	2016	24	10.7	10:14	46.2	LSG	None	60	38.4	51.3	38.4	-
Cazzo et al[31]	2018	1	25	1:0	55.0	BPD	None	12	55	-	-	-
Present study	2018	5	19.2	2:3	47.3	OAGB-MGB (2), LSG (2), RYGB (1)	None	100.8	-	49.5	25.3	−1.2

Note. Number in brackets denotes number of patient.

Abbreviations: BIB, bioenteric intragastric balloon; BMI, body-mass-index; BPD, biliopancreatic diversion; DS, duodenal switch; EWL%, percentage of excess weight loss; F, female; FU, follow-up; LAGB, laparoscopic assisted gastric banding; LSG, laparoscopic sleeve gastrectomy; M, male; OAGB-MGB, one anastomosis gastric bypass-minigastric bypass; RYGB, Roux-en-Y gastric bypass; VBG, vertical banded gastroplasty.

comparable benefit at 5 to 10 years.[30] Despite an initial improvement in T2DM and OSAS in the first 2 years, symptom rebound followed by progressive worsening was apparent after 4 to 5 years. New onset of obesity-related comorbidities like hypertension could not be delayed or prevented by bariatric surgery. Bariatric surgery failed to achieve sustainable comorbidity resolution in PWS patients by 6 to 10 years of follow-up. More importantly, premature death could not be prevented in one of our patients. PWS patients carry a risk of death 20 times higher than the general population, and majority of their deaths are due to obesity-related comorbidities in the early childhood or adolsecence.[41,42] Because surgical weight loss and comorbidity improvement could not be maintained over time, premature death was not uncommon even after bariatric surgery.[12,18,22]

As recommended by the ASMBS Pediatric Bariatric Surgery Guidelines, metabolic and bariatric surgery should be considered in PWS patients given the lack of other options in patients with hypothalamic or syndromic obesity.[43] Although control of obesity in PWS is notoriously difficult by non-operative strategies, our results of poor surgical weight loss efficacy over time do not support the routine use of bariatric surgery in PWS. As long as the phenotypic food craving manifestations are not correctable in PWS, bariatric surgery may not be a wise option given the risks of surgical and nutritional complications. Hence, our unit has stopped providing bariatric surgery service to PWS patients since 2018.

We recognize several limitations in this study. First, our patient sample of five patients was small and might not be representative for PWS in general. Because of the small sample size, comparison of different bariatric procedures for their weight loss outcomes was impossible. Second, our study did not measure the long-term changes in the hormonal profile especially the ghrelin levels. While our earlier report had demonstrated an initial significant reduction in ghrelin levels at 1 year after surgery, the corresponding ghrelin levels at longer-term follow-up were not available. Hence, it was unknown if there was rebound in the ghrelin levels at longer-term follow-up and if there was correlation with the post-operative eating behaviour.

In conclusion, bariatric surgery could not produce sustainable weight loss and comorbidity resolution in patients with PWS. Despite an initial success of weight reduction in the first 2 years, weight rebound back to the original body weight in long-term follow-up of 5 to 10 years was the main concern. Based on the findings in this study, bariatric surgery could not be recommended to patients with PWS.

CONFLICT OF INTEREST STATEMENT

No conflict of interest was declared.

AUTHOR CONTRIBUTIONS

SY Liu was responsible for study design, data collection, data analysis, data interpretation, literature search, generation of figures, and writing of the manuscript. SK Wong was responsible for study design, data collection, data interpretation, and writing of the manuscript. CC Lam was responsible for data collection, data analysis, data

interpretation, and writing of the manuscript. EK Ng was responsible for study design, data interpretation, literature search, and writing of the manuscript.

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