




Prader-Willi Syndrome: Role of Bariatric Surgery in Two Adolescents with Obesity

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Bariatric surgery (BS) is an effective treatment for adolescents with severe obesity; limited research evidence suggests that BS can be safely performed in youth with developmental delay (DD) to improve obesity-related comorbidities [1]. We report two adolescents with Prader-Willi Syndrome (PWS) who underwent BS. PWS is a multisystemic genetic disorder caused by the lack of expression of genes on the paternally inherited chromosome 15q11.2-q13 region. The three main genetic subtypes are paternal 15q11-q13 deletion (65–75%), maternal uniparental disomy 15 (20–30%), and imprinting defect (1–3%). DNA methylation is the diagnostic test detecting PWS in all three molecular genetic classes. Clinical manifestations of PWS are different according to age, ranging from hypotonia with poor suck in the first years of life to excessive weight gain, DD, and behavioral problems becoming evident in youth. The phenotype is likely due to hypothalamic dysfunction, which is responsible for hyperphagia, temperature instability, high pain threshold, hypersomnia, and multiple endocrine abnormalities including growth hormone and thyroid-stimulating hormone deficiencies, hypogonadism, and central adrenal insufficiency. The estimated prevalence is 1 in 10,000 to 30,000, equally divided in males and females [2]. Obesity is a significant contributor to mortality in PWS due to both cardiorespiratory failure caused

by sleep hypoventilation disorders, obstructive sleep apnea syndrome (OSAS), and upper airway and respiratory muscle hypotonia [3], and to diabetes. Hyperphagia-related behaviors also increase the risk for gastrointestinal (GI) perforation and necrosis, aspiration, choking, and swallowing difficulties for a combination of factors from central hypotonia, reduced GI motility, to rapid food consumption [4]. Treatment with recombinant growth hormone (rGH) therapy is effective and improves body composition, promoting motor functions in youth [5], but if patients become severely obese and if OSAS occurs, rGH should be interrupted [6].

Obesity management involves environmental control with early institution of a low-calorie and well-balanced diet, regular exercise, restriction of access to food, and counseling of the patient and family. Nonetheless, even though discussion with parents about attempts to control hyperphagia starts even during infancy, it is often insufficient to prevent morbid obesity. Treatment with BS, as gastric banding or bypass, has not been shown to reduce hyperphagia or achieve long-term weight reduction and is associated with morbidity and mortality [7].

Literature debates about BS as an option to treat morbid obesity in PWS; we point out what we got in our two cases.

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Patient 1 was diagnosed with PWS due to severe hypotonia at 3 months by DNA methylation test. The rGH therapy was started at 2 years and stopped at 7 years because of severe obesity and onset of OSAS. At 12 years (weight 100.9 kg, BMI 44.8 kg/m²), he showed severe lumbar thoracic kyphoscoliosis, and 2 years later, he developed respiratory complications that required positive pressure night ventilation (5–6 h a night). Finally, at 16 years (weight 131.5 kg, BMI 53.3 kg/m²), two consecutive seizures of respiratory failure required an intensive 1-month hospitalization; after which, the patient was referred for BS, and one anastomosis gastric bypass (OAGB) surgical treatment was performed. No complications occurred, except for transient anemia. Lung function significantly improved since the first few weeks after surgery. Seventeen months later, he had lost 25.5 kg (BMI 43 kg/m²).

Patient 2 was diagnosed with PWS due to severe hypotonia at the first month of life by DNA methylation test. He was referred to our center at 7 years, when rGH therapy was started and performed only for 2 years, because of worsening obesity and onset of OSAS. At 14 years, he developed valgus deformity on both knees with pain unresponsive to therapy and impaired walking. Magnetic resonance (MR) showed degeneration of both menisci, patellar subluxation with clicking knee, and edema in the spongy tissue of the tibial plate. At 15 years, he completely lost the ability to walk: a significant weight loss could have reduced the knee overload. Therefore, he was referred for BS, and OAGB was performed (weight 144 kg, BMI 46.22 kg/m²). No complications occurred. Six months later, weight was 122.7 kg (14.79% TWL), and BMI was 39.45 kg/m²; OSAS improved considerably, and he was able to walk again due to pain resolution and knee deformity attenuation, as confirmed by MR.

BS treatment of adolescents with obesity and DD is debated in literature. The ESPGHAN Committee Position Statement does not contraindicate surgery in these patients but expresses the need to have decision making ability and provide age-appropriate informed consent [8]. Guidelines of the American Society of Metabolic and Bariatric Surgery contraindicate this choice in patients affected by DD but indicate BS as an option when comorbidities occur in patients affected by syndromic obesity as PWS [9]. Australian and New Zealand recommendations contraindicate BS when obesity is hyperphagia-related [10]. Goldstone considers restrictive techniques ineffective to reduce hyperphagia or to achieve long-term weight reduction and associated with morbidity and mortality while considering biliopancreatic diversion effective on weight loss but more burdened with complications due to intestinal malabsorption [7]. Scheimann, regarding the 60 PWS patients who underwent BS, concludes that there is little justification to submit PWS patients to BS-related risks, given the short-term result in weight loss [11]. Alqahtani suggests that BS can be considered and indicates sleeve gastrectomy as safe and effective [12]. Matheson

presents 89 adolescents with DD, among which 70 have PWS, who underwent BS and concludes that BS is a relatively safe procedure with limited adverse complications [1]. Gibbons affirms that BS may represent an alternative way to reduce extreme obesity in patients with DD, stressing the importance of an intensive multidisciplinary approach and integrated social support system [13]. Liu et al. showed that, after initial weight reduction in the first 2 years due to BS, almost all patients returned to their original body weight in 6 years [14]. Hornack, after examining the efficacy of sleeve gastrectomy in adolescents with severe obesity and DD, affirms that BS may be a helpful tool and underlines that undergoing BS during adolescence has the advantage of a supportive caregiver [15]. PWS patients also present increased risk in anesthesia condition due to central adrenal and thyroid dysfunctions and compromised respiratory performances [16], although recent reports did not show complications directly related to anesthesia [17].

However, a hundred cases of young people with PWS who underwent BS are presented in literature [1, 18]. All cases reported are focused on the surgical technique options and their efficacy more than the role of BS in improving obesity-related life-threatening comorbidities.

The surgical technique performed in our two patients is OAGB, a mixed intervention, both restrictive and partially malabsorptive. It seems to have fewer side effects than other techniques and better results at 2 years in terms of weight loss [19, 20]. In our two patients, BS was effective in determining immediate weight loss, and both rapidly benefited from comorbidity improvement: respectively, respiratory failure and walking difficulties.

In conclusion, although most international recommendations discourage BS in PWS patients because of both increased risks and poor results in a long-term follow-up, some serious comorbidities linked to obesity force this choice as the only possibility to reduce obesity complications that could be life threatening. It might be important to set up a committee with experts from multiple disciplines to evaluate and decide on a case-by-case basis.

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Compliance with Ethical Standards

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

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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

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