

Impact of bariatric surgery on clinical outcome in LOPD

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Objective. This case study aimed to evaluate the safety and efficacy of sleeve gastrectomy surgery in an obese patient with Late-onset Pompe disease (LOPD) and to explore the potential role of bariatric surgery in improving clinical outcomes and promoting a more physiological body composition when dietary and physical interventions fail. **Methods.** We describe a case of an obese LOPD patient who underwent sleeve gastrectomy, with clinical follow-up conducted to monitor motor and respiratory functions, as well as patient-reported outcome measures (PROMs), over time. **Results.** The surgery was well-tolerated without significant complications, and prolonged stability in motor and respiratory functions was observed. Furthermore, the patient reported improvements in quality of life and PROMs following weight loss. **Conclusion.** This case suggests that bariatric surgery, specifically sleeve gastrectomy, may be a safe and effective complementary strategy for weight loss in LOPD patients, offering benefits in functional stability, and quality of life.

Key words: LOPD, BMI, bariatric surgery, ERT, complementary treatment

Introduction

Late-onset Pompe disease (LOPD) is a rare inherited metabolic disorder resulting from acid alpha-glucosidase (GAA) deficiency, which leads to a multisystemic glycogen accumulation, especially in the skeletal muscle. The characteristic clinical presentation is a limb-girdle myopathy with difficulties in climbing stairs, walking, or raising from a chair. The muscle involvement includes axial muscles, typically paraspinal muscles, proximal muscles of the lower limbs, and respiratory muscles, predominantly the diaphragm ¹. The advent of enzyme replacement therapy (ERT) following the LOTS trial ², and the development of specific guidelines for its use by the European Pompe Consortium (EPOC) ³ marked an historical change for the disease management. The ongoing development of novel treatment, encompassing next-generation ERT, gene therapy, and substrate-reduction therapy holds the potential to enhance clinical outcomes ⁴.

Dietary changes and physical exercise are also emerging as complementary interventions to counteract disease progression. In fact, many LOPD patients exhibit sarcopenic obesity, characterized by a low muscle mass and a high body fat percentage, an expression of whole body increased protein breakdown ⁵. This condition results from an increased muscle protein turnover, utilized as an alternative source of energy. Furthermore, reduced physical activity due to fatigability and muscle weakness may cause overweight. Dietary changes and regular physical activity appear to alter body composition in LOPD and help preserve lean mass (LM) ⁶.

Nevertheless, the impact of these modifications on the disease course remains a subject of debate, and treatment interventions for overweight in LOPD are not accurately delineated. When behavioural interventions fail to achieve weight loss, bariatric surgery may represent

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an alternative approach to reduce risks related to life-threatening weight-related health problems. In this context, we report the clinical outcome of an obese patient with LOPD who underwent sleeve gastrectomy surgery. We then analyzed the current literature on the relationship between the course of LOPD and body composition.

Case report

Patient

A 38-year-old man was diagnosed with LOPD for occasional myalgia, fatigability and CK elevation (400 to 690 U/l). Past medical history was unremarkable. Electrophysiological studies revealed only a right carpal tunnel syndrome and a bilateral L4-L5 radiculopathy. Muscle biopsy showed glycogen accumulation whereas on the biochemical study a severe deficit of GAA (3,8 pmol/min/mg; range $91,05 \pm 30,6$, residual activity 4.1%) was demonstrated. Genetic test confirmed LOPD diagnosis showing two heterozygous mutations in *GAA* (c.-32-13T > G/ c.1551+1G > C). Echocardiogram was normal with an ejection fraction of 60%. At the diagnosis, motor and respiratory functions were within the normal range. During the follow-up the patient gains weight up to 120 kilograms, with motor and respiratory stability over time. At age of 50, he started to complain of exertional dyspnoea and worsening of myalgia and fatigability, which limited him from climbing stairs or walking for long distances. A muscle MRI was performed showing diffuse adipose degeneration at paraspinal

muscles as well as initial signs at the thigh posterior muscles (Fig. 1). Thus, ERT was started in October 2021. At that time, his body mass index (BMI) was 40,7, and the patient consulted surgeons for a bariatric intervention. Then, he underwent sleeve gastrectomy surgery in October 2022 (weight 142 kilograms, BMI 43). Peri- and post-surgery course were free of complications. After the surgery, dietary changes were made consisting of five meals per day and multivitamin supplementation.

Methods

We conducted a comprehensive assessment of nutritional status, motor function, and respiratory function both pre- and post-bariatric surgery, with a one-year follow-up of an obese LOPD patient. Nutritional markers were assessed through laboratory tests, including evaluations of glycemic and lipid profiles, electrolytes levels, and vitamin status. Motor function was assessed through the MRC scale for strength evaluation, the 6MWD, and the GSGC score. The muscle groups examined included shoulder abductors, elbow flexors, hip flexors, and knee extensors. Respiratory function was assessed through spirometry and measurements of seated and supine Forced Vital Capacity (FVC). Motor and respiratory functions were assessed at ERT start (T0), at the time of surgery (T1) and one year after the surgical procedure (T2). Furthermore, quality of life questionnaires were administered, including The Rasch-built Pompe-specific Activity (R-PAct) and Fatigue Severity Scale (FSS), to obtain patient-reported outcome measures (PROMs). Muscle magnetic resonance imaging (MRI) including T1 and T2-STIR sequences was performed in order to assess the degree of muscle degeneration before and after treatment. To quantify muscle fat fraction (MFF), the 2-point Dixon method was used for specific muscle groups, including the gastrocnemius, posterior and anterior compartments of the thigh, gluteal muscles, lumbar paraspinal muscles, and psoas.

Results

At 1-year follow-up the patient did not show any complication following the surgical procedure. He lost about 37% of the initial weight in line with the specific type of surgery. At T0 the patient covered 513 meters in the 6MWT, and this distance remained substantially unchanged either at T1 (515 meters) or at T2 (509,5 meters). As regards the GSGC, the patient achieved the best possible score at T0 and T1, while he showed mild anserine gait and a positive Gower manoeuvre at T2, which were previously normal. It seems that weight loss unmasked anserine gait, which was more evident after the surgery. These findings were associated with a mild strength deficit of hip extensors muscles including glutei and posterior thighs muscles (MRC 4/4). Detailed outcome measures, including motor and respiratory functions, PROMs, and laboratory findings are shown in Table I. At T2, MRI showed normal muscles in the legs. There was a slight increase in MFF in the muscles of the posterior compartment of the thighs, while muscles of the anterior compartment were within normal limits. Atrophy was observed in the muscles of the anterior abdominal wall and of lumbar paraspinal muscles, with a MFF exceeding 50%, resulting the most affected muscle at ERT start whereas psoas muscles appeared normal (Fig. 1).

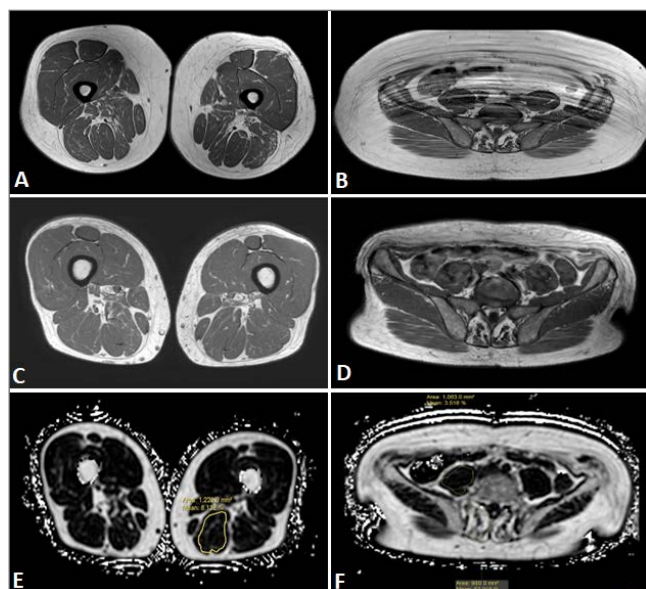


Figure 1. T0: A, B T1 weighted sequence showing initial signs of adipose degeneration of the muscle groups in the posterior compartment of the thighs on both sides (A) and hypotrophy and adipose degeneration of paraspinal muscles, particularly the spinal erector muscles and the multifidus muscle bilaterally in the lumbosacral region (B). T2: C, D T1 weighted sequence and E, F 2-point Dixon sequence showing minimal increase in MFF of the muscles in the posterior compartment of the thighs (C, E) as well as atrophy of the muscles of the anterior abdominal wall and the lumbar paraspinal muscles (MFF over 50%) (D, F).

Table 1. Demographics and functional outcome measures.

Demographics			
Age, Sex	50, M		
Age at onset	38		
Symptoms at onset	HyperCKemia, faticability, myalgia		
Muscle biopsy	Vacuolar glycogen accumulation		
GAA residual activity	4.1%		
	T₀	T₁	T₂
BMI	41.7	43.8	27.8
Laboratory			
CK (U/L)	610	361	377
Fasting glycemia (mg/dL)	91	99	99
Hb1Ac (%)	5.2	5.2	5.4
Total cholesterol (mg/dL)	214	206	219
Triglycerides (mg/dL)	114	82	94
Sodium (mmol/L)	138	141	143
Potassium (mmol/L)	3,94	4,3	4,1
Iron (mcg/dL)	103	86	75
Vitamin B12 (pg/mL)	537	1.066	559
Vitamin D (ng/mL)	34,3	34	41
Motor function			
6MWT (meter)	513	515	510
GSGC	4	4	6
Gait (score, sec)	1; 7,5	1; 7,5	2; 6,71
Stairs (score, sec)	1; 2,35	1; 2,6	1; 2,8
Gowers (score, sec)	1; 5,22	1; 3,1	2; 4,6
Chair (score, sec)	1; 1	1; 0,9	1; 1,42
Respiratory function			
FVC (liter)	4,53	4,95	5,43
FVC (%)	92	99	109
Supine FVC (liter)	4,2	5,17	5,42
FVC drop (%)	-7	4	0
PROMs			
R-PACT	33	35	36
FSS	18	18	15

T₀ ERT start; **T₁** Time of surgery, one year since ERT start; **T₂** One year after surgery.

Discussion

We investigated the efficacy, and safety of bariatric surgery in an obese patient with LOPD to also examine how weight loss may influence the disease progression.

Bariatric surgery has been reported as a safe therapeutic option in patients affected by different types of neuromuscular disorders, such as myotonic dystrophy type 1 and facioscapulohumeral dystrophy. In these patients, the restricted physical activity may lead to an increased risk of becoming overweight ⁷. When lifestyle changes were insufficient for losing weight, they appealed to bariatric surgery. Although the procedure itself does not exert a direct impact on the disease course, weight loss can mitigate fatigue and enhances the overall quality of life ^{8,9}.

To date, it has been reported that various alterations in body composi-

tion take root in Pompe disease. These include reduced bone mineral density, as evidenced through dual X-ray absorptiometry (DXA) scanning, and changes in BMI and fat mass (FM) ¹⁰. Higher BMI with higher FM is associated with muscle overload and worse motor performance. In these patients, an increase in lean mass through exercise and dietary change could improve muscle strength ⁶. BMI has also been proposed as a prognostic factor, with better treatment outcomes associated with lower BMI ¹¹. Nevertheless, the relationship between BMI and the disease appears to be quite complex. Indeed, a subset of patients with low BMI is associated with severe respiratory dysfunction and a more severe disease stage, likely due to respiratory muscle waste. This group is characterized by a worse prognosis and a poorer therapeutic response. On the other hand, ERT alone appears insufficient to reverse protein breakdown and restore a more physiological body composition ¹². The effects of bariatric surgery and weight loss leading to a significant reduction in BMI in patients with LOPD, so far, have not been reported. Our patient demonstrated clinical stability, as evidenced by motor and respiratory functions, and reported reduced fatigue following weight loss. Metabolic profiles of glucids and lipids, and the levels of electrolytes and vitamins were evaluated and no changes in these parameters were detected either before the surgery or one year after the procedure.

Interestingly, weight loss following bariatric surgery was associated with a subjective improvement in quality of life as reported by the patient. Accordingly, a reduction of FSS and R-PACT scores was observed after one year from surgery suggesting that weight loss may mitigate fatigue. However, data suggest that the restoration of a more physiological body composition may improve disease outcome and treatment response, and bariatric surgery may play an important role in achieving weight loss when other interventions fail.

Long-term study on alglucosidase alfa as ERT showed a substantial improvement during the first 2-3 years, followed by a secondary decline ¹³. Our patient underwent bariatric surgery after one year of ERT and clinical data showed stability in motor and respiratory functions over three years since ERT started suggesting a possible synergic effect of BMI reduction and ERT on patient outcome. Ravaglia et al. hypothesized that the reduction of FM increases the bioavailability of ERT, thus improving motor outcome through a more efficient targeting to skeletal muscles ¹².

A latter consideration has to be done on safety of bariatric surgery on patient with a metabolic muscle disorder because a myopathy has been reported in few obese patients as post-surgical procedure characterized by predominant weakness of the quadriceps muscle and occurring in a context of rapid and massive weight loss, slowly reversible after renutrition ¹⁴. In the case herein described that underwent sleeve gastrectomy, no peri- or post-procedural complications occurred and no progression of myopathic damage was reported during the observation time.

Conclusions

Bariatric surgery seems safe and effective in overweight LOPD patients, but a prolonged observation of such cases and a better understanding of how BMI change after surgery influences the disease course are necessary to evaluate its use as a prognostic factor.

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Conflict of interest statement

OM and AT received honoraria from Sanofi Genzyme.

Authors contributions

M.P.: collection of data and manuscript writing. A.T.: scientific review. O.M.: manuscript writing and scientific review.

Ethical consideration

This case report was conducted following ethical standards to ensure respect for the dignity and the rights of the patient involved. Written informed consent was obtained from the patient for the collection and publication of clinical data and images. The patient was informed about the nature of the study, its purposes, and the use of personal information. Measures were taken to ensure anonymity of the patient.

References

- 1 Winkel LP, Hagemans ML, van Doorn PA, et al. The natural course of non-classic Pompe's disease; a review of 225 published cases. *J Neurol*. 2005; 252:875-84. <https://doi.org/10.1007/s00415-005-0922-9>
- 2 van der Ploeg AT, Barohn R, Carlson L et al. Open-label extension study following the Late-Onset Treatment Study (LOTS) of alglucosidase alfa. *Mol Genet Metab*. 2012;107:456-61. <https://doi.org/10.1016/j.ymgme.2012.09.015>
- 3 van der Ploeg AT, Kruijshaar ME, Toscano A, et al. European consensus for starting and stopping enzyme replacement therapy in adult patients with Pompe disease: a 10-year experience. *Eur J Neurol* 2017;24:768-e31. <https://doi.org/10.1111/ene.13285>
- 4 Guémy C, Laforêt P. The new horizons for treatment of Late-Onset Pompe Disease (LOPD). *Rev Neurol (Paris)*. 2023;179:81-89. <https://doi.org/10.1016/j.neurol.2022.12.004>
- 5 Papadimas GK, Terzis G, Methenitis S, et al. Body composition analysis in late-onset Pompe disease. *Mol Genet Metab*. 2011;102:41-3. <https://doi.org/10.1016/j.ymgme.2010.09.002>
- 6 Tarnopolsky MA, Nilsson MI. Nutrition and exercise in Pompe disease. *Ann Transl Med*. 2019;7:282. <https://doi.org/10.21037/atm.2019.05.52>
- 7 Vujnic M, Peric S, Popovic S et al. Metabolic syndrome in patients with myotonic dystrophy type 1. *Muscle Nerve*. 2015; 52:273-7. <https://doi.org/10.1002/mus.24540>
- 8 Håkansson K, Kostic S, Lindberg C. Surgical treatment of obesity in DM1--a case report and a review of the literature. *Neuromuscul Disord*. 2015 ;25:414-7. <https://doi.org/10.1016/j.nmd.2015.02.002>
- 9 Abel EEDH, Cup EHC, Lanser A, et al. Experiences with bariatric surgery in patients with facioscapulohumeral dystrophy and myotonic dystrophy type 1: A qualitative study. *Neuromuscul Disord*. 2018 ;28:938-946. <https://doi.org/10.1016/j.nmd.2018.09.003>
- 10 van den Berg LE, Zandbergen AA, van Capelle CI et al. Low bone mass in Pompe disease: muscular strength as a predictor of bone mineral density. *Bone*. 2010;47:643-9. <https://doi.org/10.1016/j.bone.2010.06.021>
- 11 Ravaglia S, Danesino C, Moglia A, et al. Changes in nutritional status and body composition during enzyme replacement therapy in adult-onset type II glycogenosis. *Eur J Neurol*. 2010;17:957-62. <https://doi.org/10.1111/j.1468-1331.2010.02959>
- 12 Ravaglia S, Carlucci A, Danesino C. Prognostic factors for late-onset Pompe disease with enzyme replacement therapy: The two sides of low BMI. *Mol Genet Metab*. 2010;100:388. <https://doi.org/10.1016/j.ymgme.2010.04.005>
- 13 Harlaar L, Hogrel JY, Perniconi B et al. Large variation in effects during 10 years of enzyme therapy in adults with Pompe disease. *Neurology*. 2019 ;93:e1756-e1767. <https://doi.org/10.1212/WNL.0000000000008441>
- 14 Brisset M, Durand MC, Josif A, et al. Bariatric surgery related proximal myopathy: A partially reversible complication. *Rev Neurol (Paris)*. 2021;177:1183-1188. <https://doi.org/10.1016/j.neurol.2020.10.012>