



## **Bariatric Surgery is feasible in patients with Ehlers-Danlos Syndrome**

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## **Title: Bariatric Surgery is feasible in patients with Ehlers-Danlos Syndrome**

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Short title: Sleeve gastrectomy and Ehlers-Danlos Syndrome

Conflicts of Interest: none

## ABSTRACT

Background: Ehlers-Danlos Syndrome (EDS) is a heterogeneous disease affecting connective tissues. EDS' patients have a high susceptibility for developing anastomotic leak after visceral surgery. Although, patients with EDS can also develop severe obesity and might be referred to bariatric surgery, there is just one case report in the literature regarding the outcomes of bariatric surgery in this specific context.

Objective: To report the cases of patients with EDS and severe obesity that underwent bariatric surgery.

Setting: Five French hospitals (University Hospital of Nantes, APHP Pitié Salpêtrière Hospital, APHP Bichat Hospital, Clinique St Gregoire Rennes and Clinique Mutualiste de l'Estuaire St Nazaire).

Methods: We report the cases of seven patients with EDS and severe obesity that underwent surgery.

Results: All patients showed classical post-operative course except for one case of excessive bleeding. There was no increased pain, leak, and solid parietal healing was achieved in all patients at one month post-operatively. The percent excess weight loss at one and 6 months were respectively  $13.9 \pm 3.8\%$  and  $45.3 \pm 16\%$ .

Conclusion: Our study shows that bariatric surgery is a relevant and apparently safe surgical option to consider in severely obese patients with EDS.

Keywords: Sleeve gastrectomy; Roux-en-Y gastric bypass; Ehlers-Danlos Syndrome; Bariatric surgery; leak

## INTRODUCTION

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Ehlers-Danlos Syndrome (EDS) is a heterogeneous disease affecting connective tissues and commonly characterized by the association of skin hyperextensibility, joint hypermobility, and vascular fragility.<sup>(1,2)</sup> The prevalence is 1 out of 30.000 inhabitants for the classical type (type I and II) and 1 out of 5.000 to 20.000 in the hypermobility form (type III) with the most  
30 common type of transmission being autosomal dominant. EDS is currently classified in a system of thirteen subtypes. Classical EDS (type I and V collagen) is characterized by skin hyperextensibility and generalized joint hypermobility. Hypermobile EDS (tenascin X), the most frequent form, generalized joint hypermobility is in the foreground, but also associated with skin hyperextensibility. Vascular EDS (type III and IV collagen) is an association of  
35 severe progressive valvular heart problems (aortic and mitral valve), skin involvement and joint hypermobility. EDS patients have a high susceptibility for developing leak after any surgery.<sup>(7)</sup> Most importantly, EDS is responsible for poor wound healing.<sup>(3)</sup> It is reasonable to believe that digestive sutures and anastomoses might have a higher risk of leak in the context of EDS as observed in general surgery.<sup>(8)</sup> Obesity is a rising morbid condition, gaining  
40 epidemic characteristics, with more than one out of 20 adults being affected according to recent estimations. Patients with severe obesity (BMI>35kg/M) frequently display several comorbidities such as type 2 diabetes (T2D), high blood pressure (HBP), cardiovascular diseases and cancer. Currently, bariatric surgery emerges as the most efficient therapeutic option reserved for severe obese patients and the number of procedures increases constantly  
45 worldwide.<sup>(11)</sup> Sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) are the two most commonly used procedures in clinical practice. SG has rapidly gained a large consensus in the bariatric community with 43.6% of procedures performed worldwide between 2013 and 2017.<sup>(11)</sup> Following SG, the risk of gastric leak at one month after surgery ranges between

0.94% and 2.1% <sup>(4,5)</sup> Although, patients with EDS can also develop severe obesity and might  
50 be referred to bariatric surgery, there is just one case report in the literature regarding the  
outcomes of bariatric surgery in this specific context. <sup>(1)</sup> We report the cases of seven patients  
with EDS and severe obesity that underwent SG or RYGB.

## 55 METHODS

Patients with EDS were retrospectively searched among patients who underwent bariatric  
surgery in 5 French hospitals (University Hospital of Nantes, APHP Pitié Salpêtrière  
Hospital, APHP Bichat Hospital, Clinique St Gregoire Rennes and Clinique Mutualiste de  
l'Estuaire St Nazaire). Data were retrieved from patient's charts. All patients underwent the  
60 surgical procedure, either SG or RYGB, in expert centers after complete pre-operative  
checkup. Prior to surgery, all cases were discussed and validated in multidisciplinary team  
meetings involving bariatric surgeons, diabetes experts, nutritionists, dieticians, psychologists  
and physicians experts in EDS. The eligibility criteria were: age > 18-years old, indication for  
a bariatric surgery procedure according to the French Health Authorities (HAS) guidelines: i)  
65 obesity with a Body Mass Index (BMI)  $\geq 35$  kg/m<sup>2</sup> with secondary co-morbidities (type 2  
diabetes (TD2), high blood pressure (HBP), obstructive sleep apnea syndrome (OSA), impact  
on locomotor system), or ii) BMI  $\geq 40$  kg/m<sup>2</sup>.

### Bariatric procedures

70 The choice of the surgery type SG or RYGB took into account the patient's preference as well  
as it's the medical condition taking into account the presence of co-morbidities such as T2D  
or the presence of acid reflux prior to the surgery. All SG were performed by laparoscopic  
approach. Gastrolisis was started 4 cm away from the pylorus for antral preservation.

Gastrolysis has been defined by the gastric mobilization with vascular dissections, then the opening of lesser sac and finally the section of gastrosplenic ligament. No extensive esophageal gastric junction dissection was performed. Gastric resection was calibrated on a 39 Fr tube. Staple line strengthening, by either using reinforced gastric staples or performing a continuous oversuture, and abdominal drainage were left to the surgeons discretion.

Patients treated by RYGB will have a small gastric pouch (30 cc), an antecolic 150cm long alimentary limb, a gastro-jejunal anastomosis using a linear stapler or hand-sewn, a 50 cm biliary limb, a latero-lateral jejuno-jejunal anastomosis and closure of the mesenteric defects. In case of hiatal hernia, concomitant repair was systematically performed by reduction of the hernia and posterior suture of the diaphragmatic pillars, without any mesh reinforcement. All the centers performed this surgical technique for SG and RYGB.

#### **Clinical and biological measurements:**

Preoperative data included demographic data (age, sex, weight, height, obesity related comorbidities such as T2D, HBP, OSA) and the type of planned surgery (SG or RYGB). Pre- and postoperative weight, BMI and percentage of excess weight loss (%EWL) were recorded for each patient. EWL was expressed as percent excess BMI loss (%EBMIL) calculated as:  $((\text{initial BMI} - \text{current BMI}) / (\text{initial BMI} - 25)) \times 100$ . Ideal weight was calculated as weight for a BMI= 25 kg/m<sup>2</sup>. Past medical clinical history of EDS for each patient was recorded. All patients were followed at 1, 3, 6 and one year after surgery. All the complications were sought.

#### **Ethics:**

All patients were informed that their data would be used in the study and gave their informed signed consent. This study was validated by local ethic centers.

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**Statistical analysis:**

Quantitative results are presented in mean and standard deviation. The database was built using Microsoft Excel® (Microsoft, Redmond, Washington, United States).

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## RESULTS

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### Preoperative patient's characteristics

Seven patients (mean age was  $37 \pm 10$  years) with EDS underwent bariatric surgery between 2010 and 2019, whose clinical characteristics are displayed in Table 1. Five patients were suffering from the hypermobility (type III) type, one had the classical type (type I), and one the vascular type (type IV) which was diagnosed post-operatively. The mean body weight and BMI were respectively  $118.6 \pm 24.2$  kg and  $41.8 \pm 5.3$  kg/m<sup>2</sup>. The medical history of the patients revealed no major comorbidities related to EDS. Obesity related comorbidities were arthralgia for 5 out of 7 patients and obstructive sleep apnea for 2 patients. Two patients had already undergone laparoscopic gastric banding (LGB), followed by SG for one patient. Both cases were converted to RYGB due to insufficient weight-loss. The preoperative CT-scan or abdominal echography found fatty liver with hepatomegaly in four patients and hiatus hernia in one patient. All patients underwent oesophago-gastro-duodenoscopy which showed oesophagitis in one patient which was treated before surgery.

### Postoperative outcomes

Four patients underwent SG and three patients RYGB. In three out of seven cases, staple lines were strengthened using either a reinforced gastric staples line or performing continuous suture on the staple line. Post-operative draining was used in 4 cases. Two patients spent one day in intensive care unit, just for surveillance. All patients were able to eat starting D1, and were discharged between D3 and D7, according to the habits of the centers. The median postoperative days was 5 days [3;7]. Post-operative excessive bleeding required surgical reintervention for the patient with type IV EDS. Importantly, no late complications have been recorded during the mean follow-up of one year. The % EWL at one and 6 months were respectively  $13.9 \pm 3.8\%$  and  $45.3 \pm 16\%$ . All data are presented in Table 2.

## DISCUSSION

These seven cases show that bariatric surgery, is a relevant and apparently safe surgical option to consider in severely obese patients with non-vascular EDS. All patients except one showed classical post-operative course, without increased bleeding, pain, leak, and a solid parietal healing at one month post-operatively. The patient who required surgical  
140 reintervention due to excessive post-operative bleeding was suffering from vascular EDS (type IV), which is the most severe form and was discovered only after the bariatric surgery. Our patients presented a weight loss trajectory that is comparable to that seen in non-EDS population undergoing bariatric surgery. Due to a higher potential leak risk and an overall higher complication risk in RYGB compared to SG <sup>(10)</sup>, it seemed safer to perform SG in first  
145 intention on our patients, reserving RYGB in case of insufficient weight loss, taking as less risk as possible.

The main difference in the management of these at risk patients was the more frequent use of post-operative draining to detect an hypothetical leak. Furthermore, we reinforced the suture line in three patients (1 reinforced stapler line and two with continuous suture on the full  
150 length of the gastric section, since literature suggested a low risk of staple line hemorrhage). Indeed, the attitude adopted was trying to reduce, as much as possible, the risk of staple line leak or bleeding even though several reports show no benefit in performing such staple reinforcement.<sup>(4-6)</sup>

155 Patients with EDS are known to be at risk of gastro-intestinal issues such as hernia, diverticula, spontaneous gut perforation. Beighton et al. listed, in 1996, many possible EDS-related complications, and already noticed an extreme friability of the bowel during surgical interventions and a higher bleeding risk one week after surgery. <sup>(7)</sup> Unfortunately, there are no specific articles about the leak rate in EDS patients with another type of anastomosis, like  
160 in colo-rectal surgery. Kulas Søbørg et al. showed that EDS patients, particularly the vascular

type, are exposed to a higher risk of excessive bleeding after surgery. <sup>(9)</sup> It has been the case for our only vascular EDS patient.. Due to an overall poor wound healing, all EDS patients tend to have a higher risk of leak formation, fascial dehiscence, and incisional herniation, especially in type III EDS.<sup>(2)</sup> Although post-operative complications are more frequent in all EDS patients, there is a great heterogeneity within the different subtypes.<sup>(2)</sup> Five of our patients were suffering from hypermobility EDS (type III) and one from the classical EDS (type I and II). One patient had type IV EDS, which is related to severe and potentially fatal post-operative complications. Unfortunately, his medical condition regarding EDS was unknown before surgery and the diagnosis was made only after the procedure. If known before, the procedure would not have been performed. Our current study with a mean follow-up of one year suggest that it appears to be safe to perform LSG or RYGB on classical or hypermobility EDS patients, but not in type IV patients We acknowledge that our cohort is small,, and doesn't allow us to state any guideline.

## CONCLUSION

Classical and hypermobility EDS patients could tolerate bariatric surgery , but the procedures should be performed in expert centers and the patients closely monitored. The choice of surgery should be restricted to low leak risk surgery. However, this assessment is based on the report of only 7 patients. A larger investigation including numerous cases should confirm our conclusions.

Conflict of interest: none

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**Table 1: Patient characteristics**

BMI: Body Mass Index, SD: Standard Deviation, T2D: Type 2 Diabetes, NAFLD: Non Alcoholic Fatty Liver Disease; SG: Sleeve Gastrectomy; RYGB: Roux-en-Y Gastric Bypass; EDS: Ehlers Danlos Syndrome; LGB: Laparoscopic Gastric Banding

Patient number	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>
Age, years	28	43	37	20	47	39	48
Gender	Female	Female	Female	Female	Male	Male	Female
Initial BMI, kg/m <sup>2</sup>	42 .0	41.2	43.2	41.,9	36.3	52.4	40.7
EDS type	III	III	III	I	III	III	IV
Tobacco	No	No	No	No	No	No	No
HBP	No	No	No	No	No	No	No
T2D	No	No	No	No	No	No	No
OSA	No	No	No	No	Yes	Yes	No
Arthralgia	Yes	Yes	No	Yes	No	Yes	Yes
NAFLD	No	No	No	No	No	No	No
Oesophagitis	No	No	No	Yes	No	No	No
Anterior procédure	LGB	No	No	No	No	No	LGB, SG
Current procedure	RYGB	SG	SG	SG	SG	RYGB	RYGB

	Number (%)
Surgery type :	
- SG	4 (57%)
- RYGB	3 (43%)
Reinforced staple line	
- Yes	3 (43%)
- No	4 (57%)
Type of reinforcement	
- Reinforced gastric staples	1 (33%)
- Continuous suture	2 (77%)
Post operative drainage	
- Yes	4 (57%)
- No	3 (43%)
Complications	
- All	2 (29%)
- Clavien-Dindo > 2	1 (14%)
Hospital stay (days, mean $\pm$ SD)	4.7 $\pm$ 1.9
EWL (mean $\pm$ SD) (%)	
- 1 month	13.9 $\pm$ 3.8
- 3 months	45.3 $\pm$ 16.0

**Table 2 – Surgery characteristics**

SG : Sleeve Gastrectomy, RYGB : Roux-en-Y Gastric Bypass ; EWL : Excess Weight Loss