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ORIGINAL CONTRIBUTIONS

Effect of the EndoBarrier Device: a 4-Year Follow-up of a Multicenter Randomized Clinical Trial

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Abstract

Objective To evaluate the long-term effect of the duodenal-jejunal bypass liner (DJBL) on weight loss and glycemic control.

Background Data on the long-term effect of DJBL treatment is still missing.

Methods From 2010 to 2012, 29 patients were treated with the DJBL at center A and center B, as part of a multicenter randomized controlled trial. Prior to implantation and after removal of the DJBL, all patients underwent standardized physical examination and blood sampling. Four years after removal of the DJBL, included patients underwent standardized physical examination and blood sampling as previously performed during the initial study.

Results Out of the 29 patients, 15 patients were eligible for follow-up with a median duration of 42 months. Five patients had successfully received additional bariatric surgery. Four years after explantation of the DJBL, median weight in these 15 patients was 102.0 kg (IQR 94.0–124.6), which was not statistically significantly different from the 106.1 kg at baseline (IQR 99.0–128.4). Median BMI changed from 33.1 kg/m^2 (IQR 32.3–38.5) at baseline to 33.7 kg/m^2 (IQR 31.2–36.9) after follow-up. Patients had a TWL of 2.2% (IQR − 1.3–5.6) compared to baseline weight. None of the parameters were significantly different after follow-up compared to baseline.

Conclusions The effect of weight reduction of initial DJBL treatment seems to be diminished after 4 years of follow-up. However, larger prospective studies with long-term follow-up need to be conducted in the future.

Keywords Obesity · Abdominal surgery · Duodenal-jejunal bypass liner · Type 2 diabetes mellitus

Introduction

Obesity remains a complex condition concerning populations worldwide, despite innumerable initiatives to control this epidemic disease. Recent data from the UK reported a doubling of the number of adults suffering from obesity during the past two decades [1]. In the USA, the prevalence of obesity seems to have reached a plateau phase, still affecting roughly one third (27.0–34.9%) of the adult population [2, 3]. Obesity is associated with an increased risk of developing various physical conditions, including cardiovascular disease and diabetes mellitus [4, 5].

In most healthcare systems, treatment of obesity consists of lifestyle interventions, pharmaceutical therapy, and/or bariatric surgery. According to current guidelines, bariatric surgery is reserved for the morbidly obese, defined as a body mass index (BMI) ≥ 40 kg/m^2 or ≥ 35 kg/m^2 with obesity-related comorbidity because the benefits do not outweigh the (surgical) risks in lower BMI group [6, 7]. Recent evidence demonstrated positive effects after metabolic surgery in

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patients with class I obesity (BMI 30–34.9 kg/m^2) and diabetes or metabolic syndrome; however, long-term data needs to demonstrate if these benefits persist over time [8–10]. At the same time, several endoluminal techniques were developed to create temporary or even structural changes of the gastrointestinal tract, aiming for weight loss and improvement of comorbidity [11, 12].

The EndoBarrier System ® (GI Dynamics Inc., Lexington, MA) is an endoscopically delivered duodenal-jejunal bypass liner (DJBL) that prevents the interaction of food with digestive substances throughout the foregut. Studies evaluating the effect of the DJBL have shown that DJBL treatment results in a decrease in weight and improvement of both cardiovascular and type 2 diabetes mellitus parameters up to 1 year [13–18]. Designed as a temporary device, most data on the DJBL do not exceed results more than 1 year after removal of the device. The aim of this study is to evaluate long-term effects of the EndoBarrier system ® as DJBL on weight loss and glycemic control.

Materials and Methods

From 2010 to 2012, 29 patients were treated with the DJBL at center A and center B, as part of a multicenter randomized controlled trial [13]. Both prior to implantation and after removal of the DJBL, all patients underwent standardized physical examination and blood sampling (HbA1c, C-peptide, total cholesterol, HDL, LDL, triglycerides).

No inclusion criteria were used other than participation in and completion of the randomized controlled trial at center A or center B, as described earlier [13]. Exclusion criteria were as follows: patient loss to follow-up during the previously described RCT or patient underwent conventional bariatric surgery after DJBL treatment.

Attempts were made to contact all 29 patients once more in September 2015. Information about the study was provided via mail to the patients responsive to our attempt. Two weeks after receiving the information, the patients were contacted again and invited to visit the outpatient clinic of General Surgery of center A. Patients were screened for inclusion and exclusion criteria; all eligible patients signed written informed consent. Included patients underwent standardized physical examination and blood sampling as previously performed during the initial study [13].

The study was conducted according to the principles of the Declaration of Helsinki (64th general assembly of the WMA, Fortaleza, Brazil, October 2013) and in accordance with the guideline Medical Research Involving Human Subjects Act (WMO). The medical ethical committee of center A approved the study. The general principles of informed consent, ethics review, and data management were in line with good clinical practice (GCP).

Statistical Analysis

All data are presented as median and interquartile ranges (IQR) since data were not normally distributed. The Friedman repeated measures analysis of variance followed by Wilcoxon signed-rank test and Bonferroni correction were used to assess change over time. A p value < 0.05 was regarded as statistically significant. All statistical analyses were performed using commercially available computer software (IBM Corp., released 2012, IBM SPSS Statistics for Windows, version 21.0, Armonk, NY).

Results

Patient Characteristics

Five out of 29 patients did not respond to our request to participate in this study, and nine patients declined the request for various reasons (not satisfied after initial trial participation, $n = 3$; illness of patient, $n = 1$; illness of partner or close relative, $n = 2$; occupied in work or other, $n = 2$; no reason stated, $n = 1$). Fifteen patients visited our outpatient clinic for a long-term follow-up evaluation. Ten patients had not received any additional therapy after explantation of the DJBL; the remainder was treated with bariatric surgery because of weight gain. According to the patients, no serious adverse events were reported after these additional procedures. An overview of the results is presented in Fig. 1 and Tables 1 and 2.

Intention to Treat Analyses

Four years after DJBL treatment, four patients had a laparoscopic Roux-and-Y gastric bypass (LRYGB) and one patient

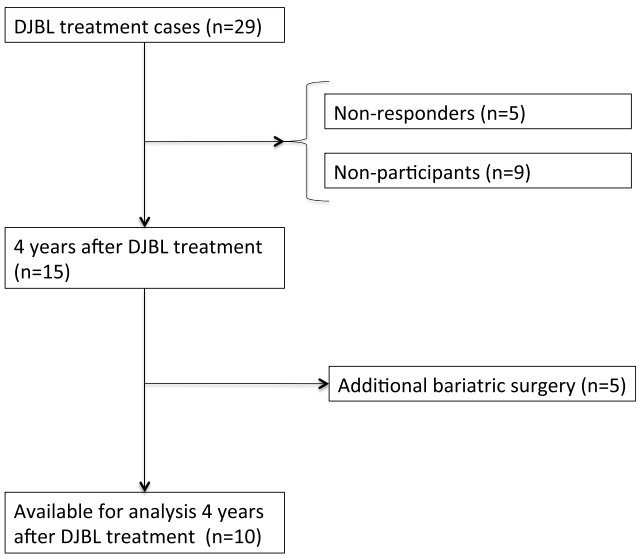

Fig. 1 Flow chart

Table 1 Change in weight (overall group, $n = 15$)

	Baseline characteristics ($n = 15$)	Directly after DJBL treatment ($n = 15$)	Long-term follow-up after DJBL treatment[a] ($n = 15$)
Weight (kg)	106.1 (99.0–128.4)	99.0 (88.4–115.5)	102.0 (94.0–124.6)
BMI (kg/m^2)	33.1 (32.3–38.5)	31.6 (30.5–35.5)	33.7 (31.2–36.9)
Total weight loss (%)	–	9.1 (4.0–13.3)	2.2 (− 1.3–5.6)

[a] Pre-operative weight outcomes have been used for the five patients who underwent additional surgery

received laparoscopic adjustable gastric banding (LAGB). Three of the five patients had DJBL treatment for 12 months; two only received DJBL treatment for 6 months. The median time from DJBL explant to additional surgery was 14 months (range 8–17). Median follow-up time from explant to trial visit for the total group was 49 months (range 40–60 months). For the intention-to-treat analyses, weight outcomes prior to additional surgery were used as "long-term follow-up outcomes" for the five patients who underwent additional surgery (median follow-up time 42 months, range 8–60). No pre-operative values were available for HbA1c or cholesterol.

There was a statistically significant difference in total body weight (and thus total weight loss and BMI) depending on treatment with the DJBL, χ^2 (2) = 14.800, $p < 0.01$.

Median weight was significantly reduced by DJBL from 106.1 kg at baseline (IQR 99.0–128.4) to 99.0 kg after DJBL treatment (IQR 88.4–115.5), $p < 0.01$. From baseline to long-term follow-up visit, the median weight changed to 102.0 kg (IQR 94.0–124.6), $p = 0.031$. This resulted in a total weight loss (TWL) of 9.1% (IQR 4.0–13.3, $p < 0.01$) during DJBL treatment, and a TWL of 2.2% (IQR − 1.3–5.6, $p = 0.031$) from baseline to long-term follow-up. BMI changed from baseline 33.1 kg/m^2 (IQR 32.3–38.5) to 31.6 kg/m^2 at explant (IQR 30.5–35.5, $p < 0.01$) and 33.7 kg/m^2 after follow-up (IQR 31.2–36.9, $p = 0.027$).

After Bonferroni correction, only the changes from baseline to explant remain statistically significant (for weight, TWL, and BMI). An overview of the results is presented in Fig. 2.

Per Protocol Analyses

Ten patients did not receive any additional therapy after explantation of the DJBL. All ten patients of this subgroup completed the initial trial with neither SAE nor complications. Five of the included patients underwent treatment with the DJBL for 6 months; the other half was treated with the DJBL during 12 months.

Within this group, there was a statistically significant difference in total body weight (and thus total weight loss and BMI) depending on treatment with the DJBL, χ^2 (2) = 8.600, $p = 0.014$. No statistically significant difference existed over time in HbA1c (χ^2 (2) = 4.222, $p = 0.121$), total cholesterol (χ^2 (2) = 0.667, $p = 0.717$), HDL (χ^2 (2) = 0.359, $p = 0.836$), or LDL (χ^2 (2) = 0.889, $p = 0.641$).

After DJBL treatment, median weight in this patient group was significantly reduced from 102.0 kg at baseline (IQR 95.0–124.4) to 93.4 kg after treatment (IQR 87.8–115.6, $p < 0.01$), and remained lower than the baseline after 4 years of follow-up with 95.2 kg (IQR 91.7–115.2, $p = 0.074$). This resulted in a total weight loss (TWL) of 6.3% during DJBL treatment (IQR 3.9–11.1, $p < 0.01$) and a remainder of 2.6% after follow-up (IQR 0.0–9.0, $p = 0.074$). BMI was 32.6 kg/m^2 at baseline (IQR 31.9–34.0) and changed from 31.2 kg/m^2

Table 2 Change in weight, glucose metabolism parameters, and cardiovascular parameters 4 years after DJBL treatment (no additional surgery, $n = 10$). Data is presented as median and interquartile ranges (IQR)

	Baseline characteristics ($n = 10$)	Directly after DJBL treatment ($n = 10$)	4 years after DJBL treatment ($n = 10$)
Weight (kg)	102 (95.0–124.4)	93.4 (87.8–115.6)	95.2 (91.7–115.2)
BMI (kg/m^2)	32.6 (31.9–34.0)	31.2 (28.8–33.0)	32.2 (30.7–33.7)
Total weight loss (%)	–	6.3 (3.9–11.1)	2.6 (0.0–9.0)
HbA1C (%)	7.8 (7.5–8.8)	7.2 (6.7–8.0)	7.6 (6.5–8.0)
Systolic blood pressure (mmHg)	141 (115–160)	131 (126–136)	143 (140–150)
Diastolic blood pressure (mmHg)	90 (80–101)	78 (74–87)	90 (88–90)
Total cholesterol (mmol/L)	3.9 (3.6–5.3)	4.0 (2.9–4.6)	3.7 (3.3–5.7)
HDL (mmol/L)	1.0 (0.7–1.2)	1.0 (0.8–1.1)	0.9 (0.8–1.3)
LDL (mmol/L)	2.1 (1.5–3.4)	1.7 (1.3–2.6)	1.9 (1.2–2.9)
Triglycerides (mmol/L)	1.90 (1.51–7.11)	1.80 (1.06–2.80)	2.25 (1.53–3.25)

during DJBL treatment (IQR 28.8–33.0, $p < 0.01$) to 32.2 kg/m^2 after follow-up (IQR 30.7–33.7, $p = 0.074$). After Bonferroni correction, only the changes from baseline to explant remain statistically significant (for weight, TWL, and BMI).

Discussion

On short term, treatment with the DJBL has proven to be both effective and relatively safe in reducing weight and improving type 2 diabetes mellitus and cardiovascular parameters compared to diet and bariatric surgery [13, 18]. DJBL treatment may function as a step-up approach for the severely obese population (BMI > 50), who need to lose weight before they can safely undergo standard bariatric surgery or for patients with DM and a lower BMI. The aim of this study was to evaluate the long-term effects of the DJBL on obesity and type 2 diabetes mellitus. With a median follow-up of 42 months after DJBL treatment, half of the patients were available for follow-up. One third of the patients initially included did not undergo additional bariatric surgery. Both with intention-to-treat analyses and per-protocol analyses, patients did not return to their initial baseline weight long after explantation of the DJBL, although no statistically significant differences were found in weight, BMI, TWL, diabetes parameters, or cardiovascular parameters compared to baseline.

Standard bariatric procedures show superior long-term results with regard to reduction in weight and comorbidities associated with obesity compared to treatment with a DJBL. A recent review on the long-term effects of laparoscopic sleeve gastrectomy (LSG) showed a reduction of EWL of > 50% after more than 5 years of follow-up [19]. RYGB showed similar results with a reported EBMI of 50–60% after one decade [20, 21]. However, as a temporary device, DJBL treatment is hard to compare to standard bariatric procedures. Despite the better results seen after bariatric surgery, a significant advantage resides in the temporary design of the DJBL procedure. Although a recent study showed that the DJBL is accompanied with adverse events in 10% of patients, removal of the device can be quickly initiated after which most adverse events resolve [22]. Koehestanie et al. [23] showed that it is feasible and safe to re-implant and explant the DJBL device resulting in significant additional weight loss. Such re-implantation of the DJBL should be considered, especially in patients that show an ongoing effect in terms of weight reduction on long term as is seen in this study.

A recent systematic review assessing the long-term effects of restricted diets as treatment of obesity showed a mean weight loss of 4.5% of their initial body weight after 4 years of follow-up ($n = 5696$) [24]. Four years after DJBL treatment, a mean weight loss of 5.2% still remained. DJBL treatment may therefore have a small advantage compared to dietary treatment on the long term regarding weight control. However, it has to be considered that there might have been a selection bias: the five patients who underwent bariatric surgery because of weight regain had a median follow-up time of only 14 months. These patients in specific might have been prone to further weight regain; however, this was not possible to investigate since they opted for surgery in mean time. Furthermore, approximately half of the patients were lost to follow-up, thereby raising the question whether the patients included in this study participated because of their positive experience with DJBL treatment.

Five of the 15 patients available for follow-up underwent bariatric surgery. No perioperative or postoperative complications occurred during and after these bariatric surgical procedures. Therefore, DJBL treatment does not seem to raise

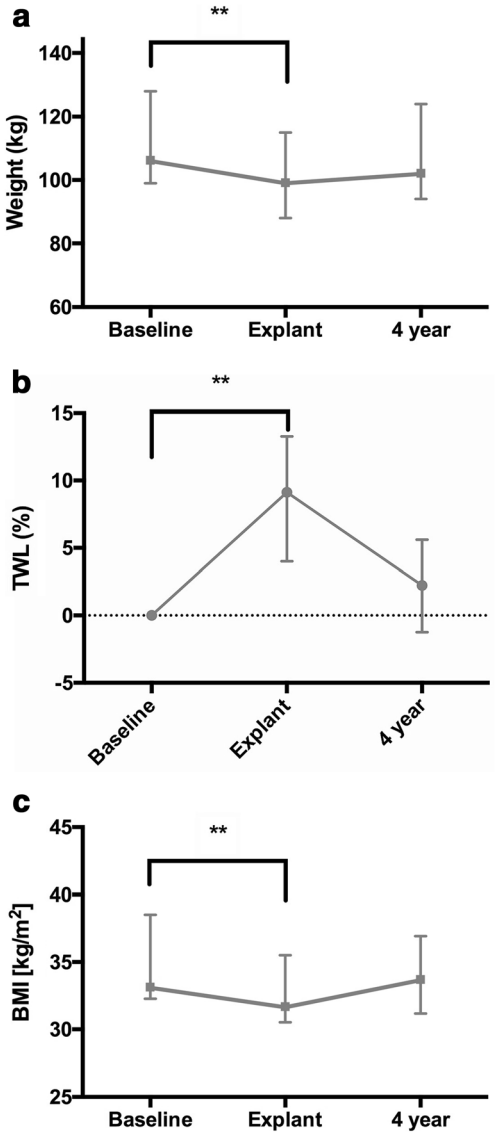

Fig. 2 **a** Change in weight (kg). **b** Change in TWL (%). **c** Change in BMI (kg/m^2). Data is presented as median and interquartile ranges (IQR). $^{**}P < 0.01$

additional issues or complicate the performance of any form of bariatric surgery.

To our knowledge, this is the first study assessing long-term follow-up after DJBL treatment. The effect of weight reduction seems to be diminished 4 years after DJBL treatment compared to baseline. Follow-up was only available for a small group of 15 patients and as mentioned before some selection bias may have played a role in the outcome seen 4 years after DJBL treatment. To fully determine the long-term effect of DJBL treatment, larger prospective studies with long-term follow-up need to be conducted in the future.

Compliance with Ethical Standards

Conflict of Interest Author 1 has no conflict of interest or financial ties to disclose.

Author 2 has no conflict of interest or financial ties to disclose.

Author 3 has no conflict of interest or financial ties to disclose.

Author 4 reports to have received grants from GI Dynamics and personal fees from GI Dynamics and is a member of the scientific advisory board of GI Dynamics since February 2017.

Author 5 has no conflict of interest or financial ties to disclose.

References

1. Health and Social Care Information Centre LS. Statistics on Obesity. England: Physical Activity and Diet; 2013. NHS, 2013 9 may 2013. Report No.: 2
2. Ogden CL, Carroll MD, Kit BK, et al. Prevalence of childhood and adult obesity in the United States, 2011-2012. JAMA. 2014;311(8):806–14.
3. Schiller JS, Lucas JW, Ward BW, Peregoy JA. Summary health statistics for U.S. adults: National Health Interview Survey, 2010. Vital Health Stat 10. Data from the National Health Survey. 2012;(252):1–207.
4. Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006 Dec 14;444(7121):840–6.
5. Van Gaal LF, Mertens IL, De Block CE. Mechanisms linking obesity with cardiovascular disease. Nature. 2006;444(7121):875–80.
6. Fried M, Yumuk V, Oppert JM, et al. Interdisciplinary European Guidelines on metabolic and bariatric surgery. Obesity Facts. 2013;6(5):449–68.
7. Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient–2013 update: cosponsored by American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery. Obesity. 2013;21(Suppl 1):S1–27.
8. Maiz C, Alvarado J, Quezada N, et al. Bariatric surgery in 1119 patients with preoperative body mass index < 35 (kg/m(2)): results at 1 year. Surg Obes Relat Dis. 2015;11(5):1127–32.
9. O'Brien PE, Dixon JB, Laurie C, et al. Treatment of mild to moderate obesity with laparoscopic adjustable gastric banding or an intensive medical program: a randomized trial. Ann Intern Med. 2006;144(9):625–33.
10. Sultan S, Parikh M, Youn H, et al. Early U.S. outcomes after laparoscopic adjustable gastric banding in patients with a body mass index less than 35 kg/m^2. Surg Endosc. 2009;23(7):1569–73.
11. Mathus-Vliegen EM. Endoscopic treatment: the past, the present and the future. Best Pract Res Clin Gastroenterol. 2014;28(4):685–702.
12. van Rijn S, Roebroek YG, Masclee AA, et al. Structural endoscopic techniques to treat obesity: a review. Surg Technol Int. 2015;26:84–91.
13. Koehestanie P, de Jonge C, Berends FJ, et al. The effect of the endoscopic duodenal-jejunal bypass liner on obesity and type 2 diabetes mellitus, a multicenter randomized controlled trial. Ann Surg. 2014;260(6):984–92.
14. Betzel B, Homan J, Aarts EO, Janssen IM, de Boer H, Wahab PJ, et al. Weight reduction and improvement in diabetes by the duodenal-jejunal bypass liner: a 198 patient cohort study. Surg Endosc. 2016.
15. Escalona A, Pimentel F, Sharp A, et al. Weight loss and metabolic improvement in morbidly obese subjects implanted for 1 year with an endoscopic duodenal-jejunal bypass liner. Ann Surg. 2012 Jun;255(6):1080–5.
16. de Moura EG, Martins BC, Lopes GS, et al. Metabolic improvements in obese type 2 diabetes subjects implanted for 1 year with an endoscopically deployed duodenal-jejunal bypass liner. Diabetes Technol Ther. 2012;14(2):183–9.
17. Gersin KS, Rothstein RI, Rosenthal RJ, et al. Open-label, sham-controlled trial of an endoscopic duodenojejunal bypass liner for preoperative weight loss in bariatric surgery candidates. Gastrointest Endosc. 2010;71(6):976–82.
18. Schouten R, Rijs CS, Bouvy ND, et al. A multicenter, randomized efficacy study of the EndoBarrier gastrointestinal liner for presurgical weight loss prior to bariatric surgery. Ann Surg. 2010;251(2):236–43.
19. Diamantis T, Apostolou KG, Alexandrou A, et al. Review of long-term weight loss results after laparoscopic sleeve gastrectomy. Surg Obes Relat Dis. 2014;10(1):177–83.
20. Edholm D, Svensson F, Naslund I, et al. Long-term results 11 years after primary gastric bypass in 384 patients. Surg Obes Relat Dis. 2013;9(5):708–13.
21. Mehaffey JH, LaPar DJ, Clement KC, et al. 10-year outcomes after Roux-en-Y gastric bypass. Ann Surg. 2016;264(1):121–6.
22. Betzel B, Koehestanie P, Aarts EO, et al. Safety experience with the duodenal-jejunal bypass liner: an endoscopic treatment for diabetes and obesity. Gastrointest Endosc. 2015;82(5):845–52.
23. Koehestanie P, Betzel B, Aarts EO, et al. Is reimplantation of the duodenal-jejunal bypass liner feasible? Surg Obes Relat Dis. 2015;11(5):1099–104.
24. Langeveld M, DeVries JH. The long-term effect of energy restricted diets for treating obesity. Obesity. 2015;23(8):1529–38.