Endoscopic Duodenal-Jejunal Bypass Liner Treatment for Type 2 Diabetes and Obesity: Glycemic and Cardiovascular Disease Risk Factor Improvements in 1,022 Patients Treated Worldwide

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There is a worldwide pandemic of type 2 diabetes (T2D) and obesity (1). In clinical practice, many patients with obesity have poor glycemic management despite diet and lifestyle advice and maximal medications (2–4). In this situation, Roux-en-Y gastric bypass is highly effective, and increased use of bariatric surgery has been recommended (2). Nevertheless, it is an invasive and irreversible surgical procedure. EndoBarrier (GI Dynamics, Boston, MA), also known as duodenal-jejunal bypass liner, is a 60-cm impermeable fluoropolymer sleeve that is implanted endoscopically into the upper part of the small intestine (2–4), left in place for up to 1 year, and then removed endoscopically. The duodenal-jejunal bypass liner was developed to mimic the proposed small-bowel mechanisms of Roux-en-Y gastric bypass (2–4) while being less invasive. In Europe in 2017, approval for use (certificate of Conformité Européenne, or CE mark) of EndoBarrier was not renewed for reasons that are not entirely clear (3,4). As over 3,000 patients have been treated with EndoBarrier worldwide, during 2017, an independent, secure, online registry was established by the Association of British Clinical Diabetologists (ABCD) for the collection of safety and efficacy data of EndoBarrier-treated patients worldwide.

By October 2022, data had been entered on 1,022 EndoBarrier-treated patients (mean ± SD age 51.3 ± 11.4 years, 52.5% male, 84.9% with diabetes, mean ± SD BMI 41.1 ± 8.7 kg/m^2) from 34 centers in 10 countries. For those with both baseline and time-of-removal data, EndoBarrier treatment was associated with considerable reduction in weight, HbA_{1c}, systolic

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Table 1—Benefits of EndoBarrier among 1,022 patients from 33 centers in 10 countries

	n	Baseline	At removal	Difference	*P* value
Impact of EndoBarrier treatment on weight, systolic BP, and cholesterol					
Weight (kg)	811	120.2 ± 25.3	106.9 ± 23.8	−13.3 ± 9.7	<0.001
BMI (kg/m^2)	808	41.2 ± 10.0	36.6 ± 8.8	−4.6 ± 3.6	<0.001
Systolic BP (mmHg)	448	135.7 ± 18.0	129.5 ± 17.0	−6.3 ± 19.2	<0.001
Cholesterol (mmol/L)	467	4.8 ± 1.2	4.2 ± 1.0	−0.6 ± 1.03	<0.001
Impact of EndoBarrier treatment on HbA_{1c} ranges (%)					
All	646	8.3 ± 1.8	7.1 ± 1.3	−1.3 ± 1.5	<0.001
HbA_{1c} 7.0–7.9	141	7.5 ± 0.3	6.8 ± 0.8	−0.7 ± 0.8	<0.001
HbA_{1c} 8.0–8.9	158	8.4 ± 0.3	7.3 ± 1.0	−1.1 ± 1.0	<0.001
HbA_{1c} 9.0–9.9	96	9.4 ± 0.3	7.8 ± 1.1	−1.6 ± 1.1	<0.001
HbA_{1c} ≥10	111	11.2 ± 1.2	8.0 ± 1.5	−3.2 ± 1.7	<0.001
Impact of EndoBarrier treatment on BMI ranges (kg/m^2)					
All	808	41.2 ± 10.0	36.6 ± 8.8	−4.6 ± 3.6	<0.001
BMI 23.0–29.9	24	28.3 ± 1.9	26.0 ± 2.2	−2.2 ± 1.9	<0.001
BMI 30.0–34.9	144	32.9 ± 1.4	29.8 ± 2.6	−3.1 ± 2.4	<0.001
BMI 35.0–39.9	253	37.6 ± 1.4	33.3 ± 2.9	−4.3 ± 2.6	<0.001
BMI ≥40	387	47.5 ± 10.4	41.9 ± 9.7	−5.5 ± 4.2	<0.001

Data are from the Worldwide EndoBarrier Registry and are mean ± SD unless otherwise specified. The centers are located in Australia, Austria, Brazil, Czech Republic, England, Germany, Israel, the Netherlands, Scotland, and Slovenia. BP, blood pressure.

blood pressure, and cholesterol (Table 1). The higher the initial HbA_{1c}, the greater the reduction (Table 1), with HbA_{1c} reduction of 3.2% (34.9 mmol/mol) when initial HbA_{1c} was ≥10.0% (86 mmol/mol). Similarly, the higher the initial BMI, the greater the reduction (Table 1). There were no differences in HbA_{1c} or weight reduction by age or sex.

There were 43 (4.2%) serious adverse events (SAE). These included early removal because of gastrointestinal bleeding in 24 patients (2.3%), liver abscess in 11 patients (1.1%) (including 8 prompting early removal and 3 found during routine explant), pancreatitis or cholecystitis in 4 patients (0.4%), and liver abscess after prolonged implant duration of more than 1 year in 2 patients (0.2%). Adverse events that were less serious occurred in 139 patients (13.6%). These included early removal because of gastrointestinal symptoms or migration or liner obstruction in 7.3% (75 patients) and precautionary hospitalization for gastrointestinal symptoms, difficult removal, or endoscopy in 6.3% (64 patients).

Data from patients both with and without diabetes was entered into the registry retrospectively, with contributors entering only the data that they had available, which is therefore incomplete. For example, some patients without diabetes did not have HbA_{1c} assessed (646 of 1,022 [63%] had HbA_{1c} assessment). This represents a limitation; the analysis is of a heterogenous group. Sufficient data to analyze the impact of EndoBarrier on diabetes medications was not available from all the centers, although one center with 62 patients reported that the device was associated with considerable reduction in insulin dose, with about 30% being able to discontinue insulin (3,4). Decrease in medication dosages and/or discontinuation of antidiabetes medication, including insulin, is a recognized benefit of EndoBarrier treatment (2).

In summary, in the worldwide EndoBarrier registry, the mean weight loss during EndoBarrier implantation was 13.3 kg (11.1% decrease in body weight from baseline), with associated improvements in glycemic control, blood pressure, and cholesterol. This reduction in microvascular and macrovascular risk factors could reduce the complications of T2D (3,4). All patients with SAE made a full recovery, and most experienced benefits despite the SAE. Some centers reported SAE that may have been avoided if patients had adhered to guidelines (3). The rate of early removal for hepatic abscess (1.1%) was noticeably less than the 3.5% rate in the original U.S. pivotal trial (2). The mechanism of hepatic abscess formation is presumably related to portal bacteremia from the device. Daily temperature monitoring (for early detection) has been added to the new U.S. pivotal study (5) to assess the effect on hepatic abscess complication. Limiting the implantation period to 9 months may also reduce the complication rate. In Europe there is currently an application for restoration of the CE mark (3). It is noteworthy that endoscopy units are ubiquitous in health care systems, as are skilled endoscopists. For the increasing numbers of patients with refractory uncontrolled T2D and obesity worldwide, there is no readily available treatment option; the potential demand is too great for available metabolic surgery resources. Therefore, if the

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safety concerns can be successfully addressed, it is possible that EndoBarrier will become widely available. There may also be a case for head-to-head comparisons of EndoBarrier with the other endoscopically implanted device, the gastric balloon.

This international registry data from a large number of patients raises the possibility that the benefits of EndoBarrier outweigh the risks. With monitoring and prompt removal of EndoBarrier if indicated, this treatment may be a useful option.

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