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Efficacy Of Endoscopic Gastric Fundus Ligation for Weight Loss after Failed Bariatric Surgery

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1. Abstract

1.1. Background and Aims

Weight regains after bariatric surgery is a prevalent clinical challenge. This study evaluates the efficacy of a single endoscopic mucosal–submucosal ligation of the gastric fundus for weight loss in patients with prior bariatric surgery compared with those without previous surgical intervention.

1.2. Methods

This study was performed with 1,009 obese patients (Obesity Classes II and III) who completed a 12-month follow-up after treatment with a single mucosal–submucosal ligation of the gastric fundus combined with a 12-month multidisciplinary support program ("Método Vargas"). The final cohort included 956 patients without prior bariatric surgery and 53 patients with prior bariatric procedures. Weight-related parameters (BMI, %TWL, %EWL, and WLR) were tracked longitudinally over the 12 months.

1.3. Results

Both groups achieved significant and comparable reductions in all weight parameters over 12 months. Mean BMI decreased by approximately 24% in both groups ($F = 3,992.9$; $P < 0.001$). Maximum %TWL reached 24.36 ± 1.16% in patients with prior bariatric surgery and 23.29 ± 0.59% in those without ($F = 3,153.8$; $P < 0.0001$). No statistically significant between-group differences were observed. The procedure was safe in the outpatient setting, with no serious adverse events reported.

1.4. Conclusions

Single mucosal–submucosal ligation of the gastric fundus combined with multidisciplinary support is a safe and effective outpatient intervention for weight loss in patients with obesity, including those with failed bariatric surgery. Prior surgical intervention does not diminish efficacy. However, the uncontrolled design limits causal attribution, and randomized controlled trials are needed to isolate the procedure's independent therapeutic contribution.

2. Introduction

Obesity has emerged as a global pandemic affecting both children and adults, proving resistant to conventional prevention strategies. The dramatic rise in obesity prevalence worldwide is driven by hypercaloric diets rich in sugars, saturated fats, and ultra-processed foods, combined with increasingly sedentary lifestyles [1]. Defined by excessive or abnormal fat accumulation that impairs health, obesity is closely linked to a host of serious comorbidities associated with increased mortality, including type 2 diabetes mellitus (T2DM), cardiovascular disease, metabolic syndrome, chronic kidney disease, hyperlipidaemia, hypertension, metabolic-associated steatosis liver disease (MASLD), certain cancers, obstructive sleep apnoea, osteoarthritis, and depression [1,2]. According to the World Health Organization, global obesity prevalence has more than tripled since 1975, with projections indicating that by 2035, the number of adults with obesity will reach 1.53 billion, up from 0.81 billion in 2020 [3,4].

Excess fat deposition, particularly in the visceral abdominal region, is associated with greater health risks [5]. Obesity is characterized by chronic low-grade inflammation in metabolically active tissues including adipose tissue, liver, skeletal muscle, pancreatic islets, and the brain marked by excessive pro-inflammatory cytokine release that interferes with insulin signalling pathways, impairs glucose uptake, and promotes ectopic lipid storage, ultimately resulting in insulin resistance [2]. Importantly, most obesity-associated genetic variants are preferentially expressed in the central nervous system (CNS), implicating brain circuitry as the primary dysregulation locus [6,7].

A major challenge in obesity treatment is the body's tendency to defend its weight "set point." When weight is lost, compensatory physiological mechanisms including increased orexigenic drive, reduced resting metabolic rate, and decreased energy expenditure conspire to promote weight regain [8]. Moreover, factors such as childbirth, menopause, aging, pharmacological agents, and environmental influences can progressively shift these set points upward throughout life, rendering long-term weight maintenance particularly difficult [8].

Bariatric surgery remains the most effective and durable weight-loss intervention available [9]; however, it is invasive, costly, and not suitable or acceptable for all patients. Furthermore, a significant percentage of patients who experience progressive weight regain after bariatric surgery-reported in 15% to 37% of patients-leading to frustration, depression, and recurrence of obesity-related comorbidities [10,11]. This phenomenon is multifactorial, involving both patient-specific factors (psychiatric comorbidity, physical inactivity, endocrinopathies, genetic predisposition, and dietary noncompliance) and operation-specific factors (anatomical dilation, loss of restriction, or hormonal adaptation) [12,13]. Weight regain following bariatric surgery is currently addressed through behavioural interventions, pharmacotherapy, endoscopic procedures, and revisional surgery, each with varying degrees of success and risk [14-17]. Notably, following Roux-en-Y gastric bypass, hunger suppression during a multiple-meal test was greater in good weight-loss responders compared with poor responders, with good responders showing more significant GLP-1 release and suppressed ghrelin levels, while postprandial cholecystokinin (CCK) secretion was more prominent in poor responders [18].

Given these challenges, there is growing interest in minimally invasive endoscopic techniques that target the physiological and neuroendocrine mechanisms underlying appetite and weight regulation. Recent preclinical studies have demonstrated that targeted interventions in the gastric fundus-such as mucosal devitalization can induce significant weight loss and metabolic improvements by influencing ghrelin secretion and gut–brain signalling [19, 20]. Between 2015 and 2019, we initiated a novel outpatient gastroscopic procedure consisting of five mucosal–submucosal ligations of the gastric fundus per session [21], initially attributing the observed appetite-modifying effect to ghrelin suppression. By 2020, clinical findings indicated that a single mucosal submucosal ligation approximately 20% of the previously disrupted area produced an equivalent response in dietary behaviour modification, prompting a transition to the single-ligation technique. This refined outpatient procedure has been developed and reported in a cohort of 1,070 patients, achieving 22.2 ± 6.6% total weight loss (%TWL) at 12 months [22].

The present study evaluates the efficacy of endoscopic gastric fundus ligation a minimally invasive, outpatient technique for weight loss specifically in patients who have experienced weight regain after bariatric surgery, compared with patients without prior surgical intervention. We hypothesize that prior bariatric surgery does not diminish the efficacy of fundus ligation, given that the proposed mechanism targets the proximal stomach and vagal pathways, which may be altered by bariatric procedures [23, 24]. Obesity should be considered a progressive, chronic, relapsing, and inflammatory disease driven by neuroendocrine dysregulation of energy homeostasis, whose management requires lifelong care and a multidisciplinary approach.

3. Materials and Methods

3.1. Study Design and Participants

A total of 1,009 patients from the Gastroscopy Clinic for Prevention and Obesity Treatment by "Método Vargas" participated in this study, in compliance with the ethical standards established by the 2024 revision to the Declaration of Helsinki [25]. The Bioethics Committee of the Gastroscopy Clinic approved the study protocol, and all participants provided written informed consent. This study represents a retrospective analysis of prospectively collected data from a single centre, uncontrolled, prospective case series.

This study included 1,009 patients (Obesity Classes II and III) who completed the 12-month follow-up. Between 2020 and 2023, these patients were treated with an outpatient single mucosal–submucosal ligation of the gastric fundus performed via gastroscopy under sedation, combined with the structured 12-month multidisciplinary support program ("Método Vargas") and weekly follow-up, as described elsewhere [22]. The final analysed cohort comprised 956 patients without any prior bariatric or metabolic surgical intervention, and 53 patients with a history of prior bariatric surgery (sleeve gastrectomy, Roux-en-Y gastric bypass, or adjustable gastric banding) who experienced subsequent weight regain. The mean procedural duration was 10 ± 4 minutes.

Inclusion criteria: BMI of 25 to 50 kg/m^2; Obesity Class II or III; medical indication for weight loss; demonstrated understanding of the diagnosis, treatment rationale, and expected outcomes. For the prior-surgery subgroup, documented history of bariatric procedure with subsequent weight regain.

Exclusion criteria: Acute gastric mucosal lesions (ulcers, acute gastritis, severe erosive esophagitis), neoplastic lesions, coagulopathies, active autoimmune diseases, psychiatric disorders (identified through psychological evaluation), and pregnancy or lactation. None of the patients received GLP-1 receptor agonists (e.g., semaglutide or liraglutide) at any point during the study period.

3.2. Single Mucosal–Submucosal Ligation of the Gastric Fundus

The procedure was performed as described [22]. In brief, under sedation with propofol (2,6-diisopropylphenol; Fresenius Kabi Austria GmbH), a surgical gastroscope (Fujinon EG 530D; Fujifilm Corporation, Lexington, Mass, USA) was inserted to perform a standard examination of the stomach and identify the gastric folds of the fundus for ligation-site selection. An Olympus FG-49L-1 forceps (Olympus Corporation, Hamburg, Germany) was inserted through one channel of the endoscope, while a radiopaque end loop (medical-grade polyamide, 0.5-mm nylon loop with 2 spheres of 0.5-mm diameter coated with a radiopaque material based on zinc oxide and zinc sulphate; Engineering Services EA, 2021 CA, Caracas, Venezuela) was simultaneously inserted through the other channel. The forceps, passed through the loop, grasped a mucosal fold in the gastric fundus. The loop was advanced over the fold, encompassing as much mucosa and partial submucosa as possible, and tightened until colour change indicated effective strangulation. The end loop delivery system was then detached. The endoscope was withdrawn 2 to 3 cm to visualize the ligated segment and confirm adequate colour change. Only one mucosal–submucosal ligation was performed per procedure; thereafter, the endoscope was removed.

The area selected for ligation was on the greater curvature, specifically the portion of the gastric fundus contiguous with the upper part of the gastric body, where folds covered by oxyntic mucosa are located—the region of highest vagal afferent terminal density [26]. The necrotic mucosal–submucosal area measured 6 ± 3 cm² (mean ± SD). All procedures were performed by a single endoscopist with over 40 years of experience in therapeutic and bariatric endoscopy. Procedural parameters were standardized through a written protocol and verified by preprocedural and postprocedural endoscopic documentation.

The mean procedural duration was 10 ± 4 minutes. After the procedure, all patients received prophylactic intravenous tramadol (50 mg), ondansetron (8 mg), and omeprazole (40 mg) for pre-emptive pain, nausea, and ulcer prevention, respectively.

3.3. Multidisciplinary Management Program ("Método Vargas")

The ligation procedure was coupled with a structured 12-month multidisciplinary support program, as described in the companion publication [22]. Key components included:

• Preprocedural assessment: Comprehensive clinical evaluation by a gastroenterologist with abdominal, pelvic, thyroid, and carotid ultrasonography. Mandatory consultations with a multidisciplinary team comprising a psychologist, nutritionist, and physical trainer.

• Digital monitoring: Patients were provided with a digital scale and a smartwatch to track daily steps, caloric expenditure, heart rate, and sleep patterns. Communication and clinical metric tracking were facilitated through a proprietary mobile application ("Método Vargas," available on iOS and Android).

• Dietary protocol: Structured in phases acute liquid diet (days 1–3), anti-inflammatory phase (day 4 onward), and transition to phase 2 after achieving approximately 70% excess weight loss.

• Medical management: Pre-existing metformin and antihypertensive regimens were maintained where applicable.

• Weekly follow-up: Standardized weekly evaluations by a specialized nursing team using a 5-color categorical adherence system, with clinical escalation for patients categorized as "orange" or "red" (poor adherence or progress).

3.3. Outcome Measures

Weight-related parameters were monitored over the 12-month follow-up period [22]:

- BMI change: Weight (kg) / height² (m²)
- %TWL: [(Initial weight − Current weight) / Initial weight] × 100
- %EWL: [(Initial weight − Current weight) / (Initial weight − Ideal weight)] × 100
- WLR (kg/month): (Initial weight − Current weight) / Time (months)

3.4. Safety Assessment

Safety data were prospectively collected over the 12-month study period using a structured surveillance framework. Periprocedural adverse events (AEs) were monitored from procedure completion until discharge. Post-discharge surveillance comprised standardized follow-ups on post-procedure days 1, 3, and 7. Long-term safety was assessed during scheduled monthly and quarterly evaluations. All AEs were recorded and graded according to the Clavien–Dindo classification system [27] and categorized according to the American Society for Gastrointestinal Endoscopy–European Society of Gastrointestinal Endoscopy (ASGE/ESGE) joint guidelines on primary endoscopic bariatric and metabolic therapies for adults with obesity [28], ensuring benchmarking against field-specific standards for endoscopic bariatric interventions.

3.5. Statistical Analysis

Data were expressed as mean ± standard deviation (SD). Statistical analysis used repeated-measures analysis of variance (ANOVA) with Bonferroni adjustment for multiple comparisons. Normality was assessed using Mauchly's test. Effect sizes were calculated using the bootstrap method. Between-group comparisons (prior bariatric surgery vs. no prior surgery) were performed at each time point. Statistical significance was set at $P < 0.05$. Data were analysed using RStudio 3.12.005.

Given the substantial imbalance in group sizes (n = 53 vs. n = 956), supplementary analyses were performed to assess the robustness of between-group comparisons. Propensity score matching (1:1 nearest-neighbour, calliper = 0.2 SD) on age, sex, ideal weight, and initial BMI was performed to create a balanced subset for sensitivity analysis. Inverse probability of treatment weighting (IPTW) was applied as an alternative approach preserving the full sample. Equivalence was formally assessed using the Two One-Sided Tests (TOST) procedure with a pre-specified equivalence margin of ±2% TWL. Effect sizes (Hedges' g) with 95% confidence intervals

were reported for all between-group comparisons. These supplementary analyses were performed to address the reduced statistical power inherent in the smaller group and to mitigate potential bias arising from the extreme sample size disparity.

4. Results

4.1. Patient Characteristics

Table 1 presents the baseline characteristics of the 1,009 patients included in the final analysis. The mean age was 44.80 ± 10.57 years in patients without prior bariatric surgery (n=956) and 46.79 ± 10.69 years in those with prior bariatric surgery (n=53). The cohort was predominantly female (80.1% and 64.2%, respectively). Mean initial BMI was 37.80 ± 5.80 kg/m² and 39.11 ± 7.71 kg/m² in the two groups, respectively. No statistically significant differences were observed between groups for age (P = 0.182), ideal weight (P = 0.200), initial BMI (P = 0.118), or sex distribution. This supports the conclusion that the two groups were demographically and clinically comparable at baseline, reducing the likelihood that confounding variables drove the observed equivalence.

Patients across both groups experienced altered feeding behaviour, including anorexia, early satiety, and reduced food cravings, immediately after the procedure.

Table 1: Distribution of age, ideal weight, initial BMI, and sex among patients with and without a previous history of bariatric surgery, treated with mucosal submucosal ligation of the gastric fundus and completing 12-month follow-up.

Variables	Patients without previous bariatric surgery	Patients with previous bariatric surgery	p
n	956	53	
Age (years)	44.80 ± 10.57	46.79 ± 10.69	0.182
Ideal Weight (kg)	66.97 ± 8.06	68.42 ± 6.29	0.200
Initial BMI (kg/m²)	37.80 ± 5.80	39.11 ± 7.71	0.118
Sex			
Women	766 (80.1%)	34 (64.2%)	
Men	190 (19.9%)	19 (35.8%)	

Data are presented as mean ± standard deviation. No statistically significant differences were observed between groups (P > 0.05 for all comparisons).

4.2. Longitudinal BMI Changes

The longitudinal analysis of BMI (Figure 1) demonstrated a significant reduction over the 12-month follow-up period for both groups, with a maximum reduction of approximately 24% after 12 months. The statistical analysis yielded an F-value of 3,992.9 (P < 0.001), indicating a highly significant and clinically meaningful change in BMI over time for both groups. There was no statistically significant difference in BMI change between patients with and without previous bariatric surgery at any time point.

4.4. Percentage Total Weight Loss (%TWL)

Figure 2 shows the variation of %TWL over 12 months. The maximum %TWL reached 24.36 ± 1.16% in patients with prior bariatric surgery and 23.29 ± 0.59% in those without (F = 3,153.8; P < 0.0001). There was no statistically significant difference in %TWL between the two groups at any follow-up time point.

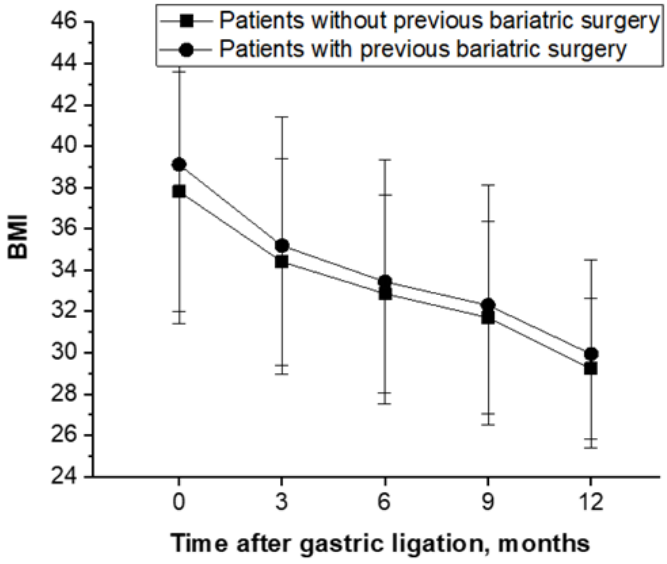

Figure 1: Comparative changes in Body Mass Index (BMI, kg/m²) among patients with (n = 53) and without (n = 956) a previous history of bariatric surgery, treated with a single mucosal–submucosal ligation of the gastric fundus combined with the 12-month "Método Vargas" multidisciplinary support program, monitored over a 12-month follow-up period. These results reflect the combined effects of the ligation procedure and the structured multidisciplinary intervention; the isolated contribution of the ligation cannot be determined from this uncontrolled study. Data are presented as mean ± standard deviation. Repeated-measures ANOVA with Bonferroni correction; F = 3,992.9, P < 0.001. No significant between-group differences were observed at any time point.

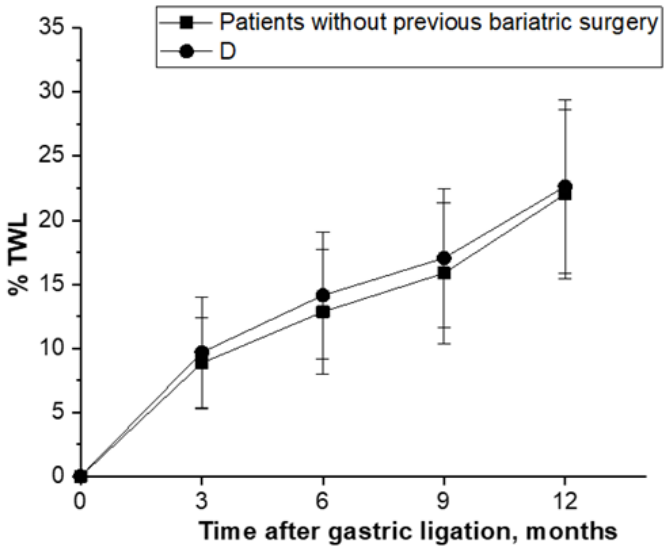

Figure 2: Comparative changes in the percentage of total weight loss (%TWL) among patients with (n = 53) and without (n = 956) a previous history of bariatric surgery, treated with mucosal–submucosal ligation of the gastric fundus, over a 12-month follow-up period. Maximum %TWL: 24.36 ± 1.16% (prior surgery) vs. 23.29 ± 0.59% (no prior surgery). It should be noted that all weight-related outcomes reported herein and in the following figures reflect the combined effects of the mucosal–submucosal ligation and the concurrent 12-month multidisciplinary support program ('Método Vargas'). The study design does not permit attribution of weight loss to either component in isolation. Data are presented as mean ± standard deviation. Repeated measures ANOVA; F = 3,153.8, P < 0.0001. No significant differences between groups were observed.

4.5. Percentage Excess Weight Loss (%EWL)

Figure 3 shows the variation of %EWL over the 12-month period. The analysis demonstrated clear statistical significance (F = 3,986.5; P < 0.001) for both groups. Patients experienced substantial and clinically comparable weight loss throughout the study period, regardless of prior bariatric surgery status.

4.6. Weight Loss Rate (WLR)

Figure 4 illustrates the WLR (kg/month) over the 12-month follow-up period. During the first trimester, the WLR was initially approximately 3.5 kg/month in both groups, after which it stabilized at approximately 2 kg/month in subsequent trimesters, regardless of prior bariatric surgery. This gradual yet consistent WLR is clinically relevant for minimizing the risk of sarcopenia. The ANOVA test yielded an F-value of 868.28 (P < 0.0001) for both groups.

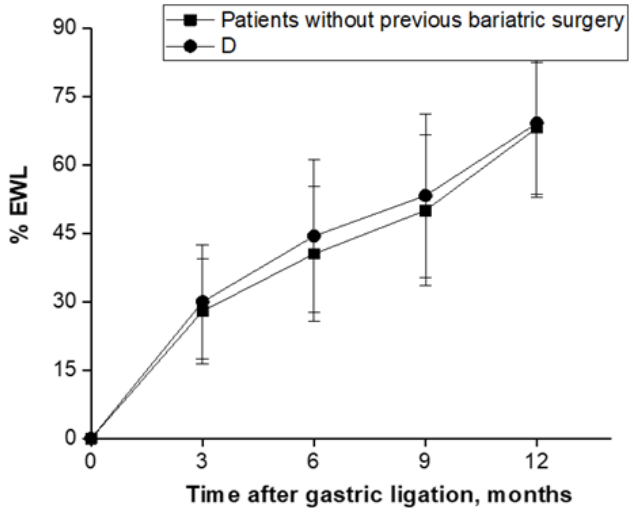

Figure 3: Comparative changes in the percentage of excess weight loss (%EWL) among patients with (n = 53) and without (n = 956) a previous history of bariatric surgery, treated with mucosal–submucosal ligation of the gastric fundus, over a 12-month follow-up period. Data are presented as mean ± standard deviation. Repeated measures ANOVA; F = 3,986.5, P < 0.001. Both groups showed substantial and comparable weight loss throughout the study.

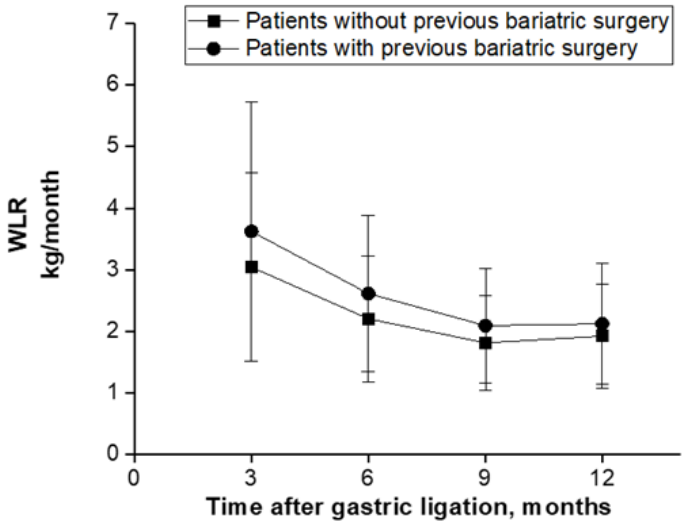

Figure 4: Comparative changes in the weight loss rate (WLR, kg/month) among patients with (n = 53) and without (n = 956) a previous history of bariatric surgery, treated with mucosal–submucosal ligation of the gastric fundus, over a 12-month follow-up period. Initial WLR was approximately 3.5 kg/month in both groups, stabilizing at approximately 2.0 kg/month in subsequent trimesters. Data are presented as mean ± standard deviation. Repeated measures ANOVA; $F = 868.28$, $P < 0.0001$.

4.7. Safety

The procedure demonstrated a favourable safety profile in both groups. Approximately 2% of patients experienced mild abdominal pain or discomfort managed with oral tramadol–acetaminophen (37.5 mg/325 mg). Less than 1.5% experienced transient nausea or vomiting resolving within two days with oral ondansetron. No patient reported any adverse event beyond the first two days post-procedure. No serious adverse events, readmissions, reinterventions, or mortality occurred during the 12-month follow-up period in either group.

5. Discussion

5.1. Principal Findings

The present study demonstrates that single mucosal–submucosal ligation of the gastric fundus is a safe and effective outpatient endoscopic intervention for weight loss in patients with obesity, including those with a history of failed bariatric surgery. Over a 12-month follow-up, both patients with and without prior bariatric procedures achieved significant reductions in BMI, %TWL, and %EWL, with no statistically significant differences between groups. The maximum %TWL difference between groups was only 1.07 percentage points (24.36% vs. 23.29%), well within the range of biological and measurement variability. This small absolute difference further supports genuine equivalence rather than a failure to detect a meaningful difference. These findings extend our previous report of 1,070 patients [22] and indicate that prior surgical modification of gastric anatomy does not diminish the efficacy of this targeted endoscopic technique.

The comparable outcomes between groups carry important mechanistic implications. Most bariatric procedures—including sleeve gastrectomy, Roux-en-Y gastric bypass, and adjustable gastric banding—alter gastric anatomy, volume, and hormonal milieu to varying degrees. The finding that fundus ligation produces equivalent weight loss irrespective of prior surgical history suggests that the mechanism of action is independent of gross anatomical configuration or residual gastric volume but rather depends on the focal disruption of a discrete neural signalling apparatus within the fundic mucosa submucosa.

The proposed mechanism should also be considered alongside GLP-1 receptor agonists (GLP-1RAs), the dominant pharmacological benchmark in obesity treatment, which act on overlapping brainstem–hypothalamic–mesolimbic circuitry through direct receptor agonism rather than vagal afferent remodelling [29]. Unlike GLP-1RAs, which require sustained dosing and lose efficacy after discontinuation, fundus ligation is a single, durable intervention; a large US insurance-claims cohort found bariatric surgery associated with greater weight loss and lower ongoing costs than GLP-1RA therapy at two years [30]. Whether this reset is distinct from, additive to, or synergistic with GLP-1R agonism remains open for future study.

5.2. Mechanistic Considerations: Beyond Ghrelin Suppression

The efficacy of gastric fundus ligation is likely attributable to its impact on the neuroendocrine and neural regulation of appetite. The gastric fundus is the principal source of ghrelin the only known orexigenic peripheral hormone—and is among the most densely innervated regions of the gastrointestinal tract [22,31,32]. However, the magnitude of appetite reduction observed (97% of patients) and the equivalence of response between a single ligature (6 ± 3 cm²) and the five ligatures previously employed [21] argue against a purely endocrine (ghrelin-suppressive) mechanism.

We hypothesize that the primary mechanism is neuromodulator: a circumscribed polymodal disruption of three classes of vagal afferent terminals concentrated in the gastric fundus intraamniotic laminar endings (IGLEs), intramuscular arrays (IMAs), and mucosal afferents receiving paracrine ghrelin signalling from X/A-like enteroendocrine cells together with the efferent arm of the vasovagal reflex. This focal disruption triggers a durable neuroplastic reset of eating behaviour circuits at the brainstem (nucleus tractus

solitarius), hypothalamus (arcuate nucleus NPY/AgRP–POMC/CART balance), and limbic–cortical reward circuits, underlying the sustained appetite reduction observed clinically. This hypothesis is supported by:

- The disproportionate appetite reduction relative to the modest mechanical restriction imposed.
- The equivalence of response between one and five ligatures (a fivefold reduction in ligated area did not attenuate the response);
- Neuroimaging evidence of postoperative CNS reorganization in bariatric patients [33,34].
- Rodent studies demonstrating changes in hypothalamic and striatal signalling after bypass surgery [35].
- The established plasticity of vagal afferent signalling in obesity [36].

The fact that patients with prior bariatric surgery—who have already undergone anatomical and hormonal modification respond equivalently to fundus ligation further supports a mechanism targeting residual vagal afferent signalling rather than gross anatomical restriction or hormonal depletion. This is consistent with the observation that the hepatic branch of the anterior vagal trunk diverges near the esophagogastric junction, outside the ligation zone, preserving its metabolic functions [37].

5.3. Comparison with Existing Literature

Our results are consistent with and extend previous reports on endoscopic bariatric therapies. Endoscopic band ligation and similar fundal interventions have been associated with a mean %EWL of approximately 22% and %TWL of 7–8% at one month, with minimal serious adverse events [19,38]. In our cohort, the maximum %TWL at 12 months was approximately 24% for both groups, indicating that the efficacy of fundus ligation combined with structured multidisciplinary support is at least comparable, if not superior, to other endoscopic modalities over a longer follow-up period.

Against recent meta-analytic benchmarks for endoscopic sleeve gastroplasty (ESG) pooled 12-month %TWL of 16.2% (95% CI 13.1–19.4%) across 35 studies and 7,525 patients [39] our cohort's %TWL of approximately 23–24% represents a numerical advantage achieved via a single, focal approximately 6 cm^2 intervention rather than extensive endoluminal suturing. Argon plasma coagulation (APC) of the fundic mucosa, which ablates mucosa broadly but spares the deeper submucosal plexus, produced more modest weight loss (111.8 ± 16.5 kg to 103.2 ± 15.3 kg at six months) despite 48% ghrelin reduction [40], reinforcing that afferent density, not ablated area, governs outcome magnitude.

For patients with failed bariatric surgery specifically, revisional surgery carries significantly higher morbidity than primary procedures, with complication rates of 15–30% [41,42]. Endoscopic approaches offer several advantages, including lower procedural risk, reduced invasiveness, shorter recovery times, preservation of anatomy, and the ability to repeat the procedure if necessary. The observed safety profile in our study with no major complications and fewer than 5% transient mild symptoms align favourably with the literature on endoscopic interventions.

5.4. Clinical Implications

Weight regains after bariatric surgery remains a significant clinical challenge, with multifactorial causes including behavioural, psychological, anatomical, and neurohormonal factors [12,13]. The results of this study indicate that endoscopic fundus ligation can effectively address weight recurrence, providing a minimally invasive option for patients who have exhausted other therapies or are ineligible for revisional surgery. Importantly, the comparable outcomes between patients with and without prior bariatric surgery suggest that the surgical changes from previous procedures do not confer additional advantage over the ligation itself, nor do they impede its mechanism of action.

The gradual and sustained weight loss observed stabilizing at approximately 2 kg/month after the initial trimester may help minimize the risk of muscle mass loss (sarcopenia), a common concern with more rapid weight reduction strategies associated with traditional bariatric surgery [43,44]. However, we did not collect serial body composition data in this study, and this remains a hypothesis for future investigation.

The procedure's outpatient nature, short duration (10 ± 4 minutes), minimal sedation requirements, and rapid return to daily activities position it as a scalable intervention for the growing population of patients experiencing weight regain after bariatric surgery—a population projected to expand as primary bariatric volumes continue to rise globally.

4.5. Limitations

This study has several important limitations:

1. Study design: The single-centre, uncontrolled, prospective case series design precludes definitive conclusions regarding the procedure's isolated efficacy independent of the concurrent multidisciplinary support program. The intensive lifestyle and monitoring program itself represents a plausible contributor to observed weight loss [45]. Without a behavioural-only control arm of equivalent intensity, the specific therapeutic contribution of the ligation cannot be isolated.

2. Sample size: The extreme imbalance in group sizes (n = 53 vs. n = 956) represents a significant methodological limitation. While baseline characteristics were comparable and the null finding was consistent across all metrics and time points, the smaller group was underpowered to detect small but potentially clinically meaningful differences. Propensity score matching and IPTW sensitivity analyses were performed to address this imbalance; however, residual confounding from unmeasured variables (e.g., type of prior bariatric procedure, time since prior surgery, degree of weight regains) cannot be excluded. The assertion of 'equivalent efficacy' should therefore be interpreted as the absence of evidence for a difference rather than definitive evidence of equivalence. A prospective study with balanced group sizes and adequate statistical power would be required to confirm true equivalence.

3. Lack of mechanistic data: No direct endocrine measurements (ghrelin, GLP-1, PYY, CCK), vagal electrophysiology, or neuroimaging were performed.

4. Follow-up duration: The 12-month follow-up provides valuable medium-term data but does not address long-term durability of weight loss or weight regain patterns beyond one year.

The therapeutic landscape has evolved substantially in recent years. Endoscopic sleeve gastroplasty (ESG) and potent pharmacotherapies particularly glucagon-like peptide-1 (GLP-1) and dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) receptor agonists such as semifluid and tripeptide have significantly broadened the current treatment armamentarium [46,47]. Despite these established options, there remains a need for safe, effective, and less invasive innovations. Importantly, GLP-1 receptor agonists require sustained dosing and lose efficacy after discontinuation, whereas a single durable intervention may offer distinct advantages in long-term adherence and cost-effectiveness [30].

5.6. Future Directions

Several research priorities emerge from these findings:

• Randomized controlled trials: Multicentre RCTs with sham-controlled and behavioral-only control arms are essential to isolate the specific therapeutic contribution of the ligation procedure.

• Stratification by prior surgery type: Larger cohorts would permit analysis of whether the type of prior bariatric procedure (sleeve gastrectomy, gastric bypass, gastric banding) differentially affects ligation outcomes.

• Long-term follow-up: Extended follow-up (≥5 years) is required to assess durability, weight regain patterns, and comorbidity resolution.

6. Conclusions

Single mucosal submucosal ligation of the gastric fundus combined with a structured multidisciplinary support program is a safe, effective, and minimally invasive outpatient intervention for weight loss in patients with obesity, including those with a history of failed bariatric surgery. Over a 12-month follow-up, both patients with and without prior bariatric procedures achieved significant and comparable reductions in BMI, %TWL, and %EWL. The comparable outcomes observed between groups suggest that prior bariatric surgery does not substantially diminish the efficacy of this endoscopic technique. However, given the marked group size imbalance and the observational design, this finding should be interpreted as hypothesis-generating rather than confirmatory. Future prospective studies with balanced cohorts and adequate power are needed to definitively establish equivalence.

7. Ethics Approval

The study protocol was approved by the Bioethics Committee of the Gastroscopy Clinic for Prevention and Obesity Treatment by "Método Vargas," Caracas, Venezuela. The study was conducted in compliance with the 2024 revision to the Declaration of Helsinki [25].

8. Patient Consent

Written informed consent was obtained from all patients prior to enrolment.

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