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REVIEW ARTICLE

Endoscopic Treatment of Weight Regain Following Roux-en-Y Gastric Bypass: a Systematic Review and Meta-analysis

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Abstract Roux-en-Y gastric bypass (RYGB) is the most commonly performed bariatric procedure. Despite its high efficacy, some patients regain part of their lost weight. Several endoscopic therapies have been introduced as alternatives to treat weight regain, but most of the articles are relatively small with unclear long-term data. To systematically assess the efficacy of endoscopic therapies for weight regain after RYGB. We searched MEDLINE, EMBASE, Scopus, Web of Science, Cochrane, OVID, CINAHL/EBSCo, LILACS/Bireme, and gray literature. Primary outcomes were absolute weight loss (AWL), excess weight loss (EWL), and total body weight loss (TBWL). Thirty-two studies were included in qualitative analysis. Twenty-six described full-thickness (FT) endoscopic suturing and pooled AWL, EWL, and TBWL at 3 months were 8.5 ± 2.9 kg, 21.6 ± 9.3%, and 7.3 ± 2.6%, respectively. At 6 months, they were 8.6 ± 3.5 kg, 23.7 ± 12.3%, and 8.0 ± 3.9%, respectively. At 12 months, they were 7.63 ± 4.3 kg, 16.9 ± 11.1%, and 6.6 ± 5.0%, respectively. Subgroup analysis showed that all outcomes were significantly higher in the group with FT suturing combined with argon plasma coagulation (APC) ($p < 0.0001$). Meta-analysis included 15 FT studies and showed greater results. Three studies described superficial-thickness suturing with pooled AWL of 3.0 ± 3.8, 4.4 ± 0.07, and 3.7 ± 7.4 kg at 3, 6, and 12 months, respectively. Two articles described APC alone with mean AWL of 15.4 ± 2.0 and 15.4 ± 9.1 kg at 3 and 6 months, respectively. Full-thickness suturing is effective at treating weight regain after RYGB. Performing APC prior to suturing seems to result in greater weight loss. Head-to-head studies are needed to confirm our results. Few studies adequately assess effectiveness of other endoscopic techniques.

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Abbreviations

RYGB	Roux-en-Y gastric bypass
GJA	Gastrojejunal anastomosis
APC	Argon plasma coagulation
TORe	Transoral outlet reduction
PROSPERO	International Prospective Register of Systematic Reviews
BMI	Body mass index
AWL	Absolute weight loss
EWL	Excess weight loss
TBWL	Total body weight loss
SD	Standard deviation
SE	Standard error
ST	Superficial thickness
FT	Full thickness
FTS	Full-thickness endoscopic suturing
FTS-APC	Full-thickness endoscopic suturing plus argon plasma coagulation
OTSC	Over-the-scope clip

Background and Aims

Obesity is a rising pandemic. As of 2014, 13% of adults worldwide were obese, with the most affected region being the American continent [1].

Traditionally, lifestyle modification and bariatric surgery have been the recommended approaches for treatment of obesity. Lifestyle modification was non-invasive but was associated with minimal and less durable weight loss of 3 to 5% [2]. As a result, bariatric surgery has been increasingly performed worldwide, with Roux-en-Y gastric bypass (RYGB) being the most commonly performed procedure (45% of all bariatric cases) [3]. Despite its high efficacy of approximately 35.8% weight loss at 1 year and 27.7% weight loss at 10 years, RYGB patients unfortunately regain part or most of their lost weight by 10 years [4–6].

Weight regain is a common long-term complication of RYGB and is thought to be multifactorial. In addition to genetic, psychologic, and behavioral factors, dilation of the gastrojejunal anastomosis (GJA) has been shown to contribute to weight regain [7–10]. Traditionally, a revisional surgery to reduce the size of GJA may be offered to patients with weight regain. However, these procedures are invasive and carry an even higher complication rate than that of a primary procedure [11].

More recently, several endoscopic therapies to reduce the GJA size have been introduced as an alternative to treat weight regain. These include endoscopic sclerotherapy, argon plasma coagulation (APC), and transoral outlet reduction (TORe) using a plication device, a suturing device, or an over-the-scope clip [12–16]. While previous studies have shown some efficacy of these procedures, most were relatively small with unclear long-term data. This study aimed to systematically assess the efficacy of endoscopic therapies for weight regain after RYGB.

Materials and Methods

Data Sources and Searches

We thoroughly searched MEDLINE, EMBASE, Scopus, Web of Science, Cochrane, OVID, CINAHL/EBSCo, LILACS/Bireme, and gray literature from inception to October 31, 2016. The search strategy for MEDLINE was "(Bariatric* OR Gastric Bypass OR Gastroileal Bypass OR Gastrojejunostomy OR Gastrojejunostomies) AND (Endoscopy OR Endoscopic OR Endolum* OR Transoral*)". A similar search strategy was used for other databases. The study was registered on the International Prospective Register of Systematic Reviews—University of York (PROSPERO) (Registry Number CRD42016046676) (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016046676). Additionally, the study was approved by our institution's Internal Review Board (IRB number 433/16).

Literature screening was independently performed by two authors. Disagreement regarding final study inclusion was resolved by discussion. If a consensus could not be reached, the senior author (E.M.) served as the final arbiter.

Study Selection

Randomized clinical trials, observational cohort studies, and case series were considered eligible. Conference abstracts were also included if they met the eligibility criteria listed below. Reviews, editorials, case-control studies, and studies using non-human subjects were excluded, as were articles without English translation. Specific inclusion and exclusion criteria are summarized below:

Inclusion Criteria

- Studies that included patients with RYGB who presented with weight regain
- Studies that reported weight loss efficacy of endoscopic therapy for weight regain following RYGB

Exclusion Criteria

- Studies that did not describe the endoscopic method clearly

- Studies with follow-up weight or BMI less than 1 month
- Studies with endoscopic treatment for other indications besides weight regain, such as dumping syndrome or fistula closure
- Studies that did not report baseline BMI
- Studies that included patients with weight regain who had already undergone other endoscopic or surgical treatment of weight regain

Currently, there is no consensus regarding the definition of weight regain [17]. Our eligibility criteria include all articles that reported weight regain. We extracted the amount of weight regained from nadir and analyzed it with Comprehensive Meta-Analysis Software (Englewood, NJ).

The risk of bias for observational and cohort studies was assessed using the Joanna Briggs Institute Critical Appraisal Checklist for Case Series [18]. Clinical trials and cohorts can be assessed for quality of the study, but there is no consensus on how to assess the quality of studies with no control arm [19]. Therefore, studies were enrolled based on completeness of data and eligibility criteria.

Outcomes

The primary outcomes were absolute weight loss (AWL), excess weight loss (EWL), and total body weight loss (TBWL) after the endoscopic therapies for weight regain. Absolute weight loss is defined as the lost weight expressed in kilograms (kg). This was calculated using the following formula: weight prior to TORe − follow-up weight. Excess weight loss is defined as the percentage loss of the weight above BMI 25 kg/m^2 for each individual. This was calculated using the following formula: (weight prior to TORe − follow-up weight) / (weight prior to TORe − ideal weight) × 100%. Total body weight loss is defined as the percentage that the absolute weight loss represents to the baseline weight. This was calculated using the following formula: (weight prior to TORe − follow-up weight) / weight prior to TORe × 100%. Outcomes were reported using difference of means. In this study, short-, mid-, and long-term were defined as less than 3, 3–12, and 12 months or longer, respectively. If the included study reported follow-up weights at more than one time points, the one closest to 3, 6, or 12 months was chosen for the analysis.

Data Synthesis and Analysis

For the qualitative analysis, total mean AWL/EWL/TBWL was calculated using the weighted average of AWL/EWL/TBWL of each study. If the study did not specify the number of patients at the time of follow-up, an intention-to-treat analysis was used based on the baseline sample size. A comparison of weighted arithmetic means was performed using Student's *t* test.

For the quantitative analysis, only studies that reported mean AWL, EWL, and/or TBWL with standard deviation (SD) or standard error (SE) and the sample size at time of follow-up were included. If the study provided a range as a measure of variance, SD was estimated based on mathematical formulas [20]. The analysis was performed using Comprehensive Meta-Analysis (Englewood, NJ). A forest plot was built in Excel, as instructed by Derzon JH et al. [21].

Results

A total of 13,594 records were identified on the initial search. After removal of duplicates, 11,097 records were reviewed. After title/abstract assessment, 100 articles were selected for full evaluation. After individual review, 32 studies satisfied the inclusion and exclusion criteria and were included in the study (Fig. 1).

Part I: Qualitative Analysis

Of the 32 included studies, 26 described full-thickness (FT) endoscopic suturing, 3 described superficial-thickness (ST) endoscopic suturing, 2 described argon plasma coagulation (APC), and 1 described over-the-scope clip (OTSC). No study regarding sclerotherapy fulfilled eligibility criteria.

Twenty-six studies [12, 22–46] that described FT endoscopic suturing included a total of 1148 patients. Of these, seven studies, which included 320 patients, evaluated FT endoscopic suturing combined with APC (FTS-APC). The remainder 19 studies with a total of 828 patients evaluated FT endoscopic suturing alone without APC (FTS). Average baseline BMI was 38.1 ± 2.3 and 40.5 ± 2.4 kg/m^2 in the FTS-APC and FTS groups, respectively. At every follow-up time point, the average of mean AWL, EWL, and TBWL was higher in the FTS-APC group compared to that in the FTS group (Table 1).

Three studies [12, 47, 48] with a total of 127 patients described superficial-thickness endoscopic suturing. Average baseline BMI was 39.1 ± 1.4 kg/m^2. At 3, 6, and 12 months, the average of mean AWL was 3.07 ± 3.81, 4.44 ± 0.07, and 3.72 ± 7.42 kg, respectively. Two studies provided EWL data at 6 months, and the average of the mean EWL was 11.3 ± 5.5%. At 12 months, only one study provided follow-up data and the mean EWL was 9.1 ± 2.3%.

Two studies [14, 49] including 70 patients described APC. Average baseline BMI was 35.91 ± 0.7 kg/m^2. At 3 months, only one of the two studies with 30 patients [14] presented results, with mean AWL of 15.4 ± 2 kg. The remainder study with 40 patients [49] reported mean AWL at 6 months of 15.4 ± 9.1 kg.

Fig. 1 PRISMA chart

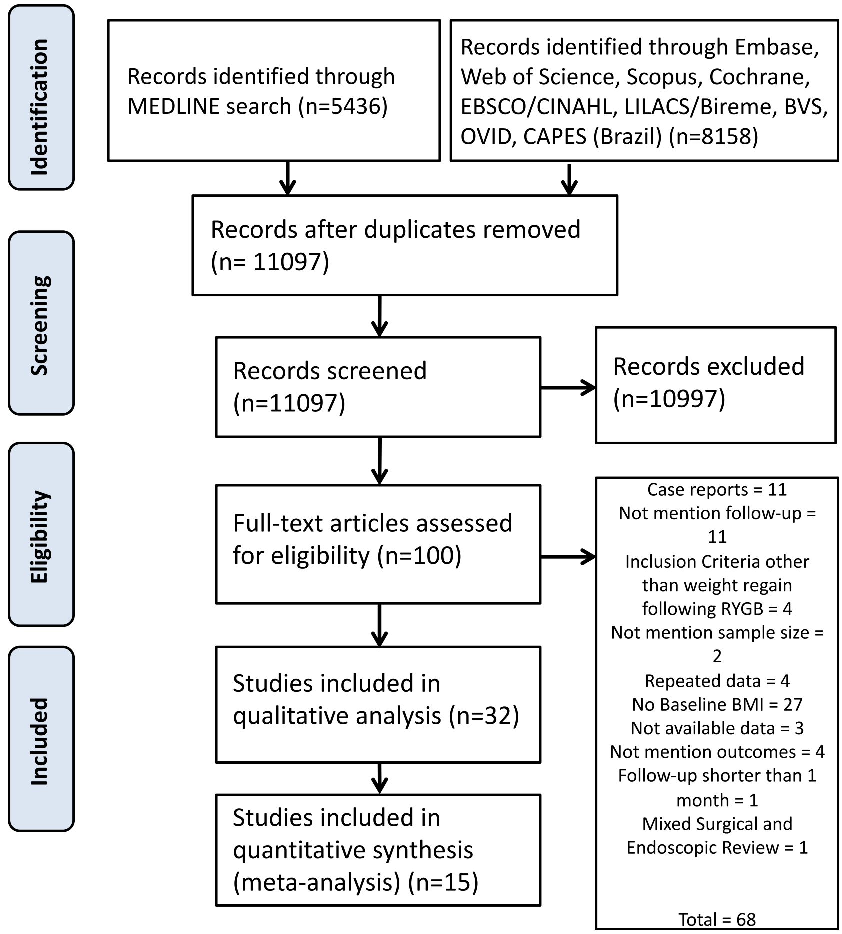


Table 1 Results of qualitative analysis at short-term, mid-term, and long-term follow-ups in patients who underwent full-thickness endoscopic suturing with APC (FTS-APC), full-thickness endoscopic suturing alone (FTS), superficial endoscopic suturing (ST), ablation with argon plasma coagulation (APC), or OTSC therapy for weight regain

	Short-term (≤ 3 months)		Mid-term (3–12 months)		Long-term (≥ 12 months)	
	Mean absolute weight loss (*n*)		Mean absolute weight loss (*n*)		Mean absolute weight loss (*n*)	
FTS	6.61 kg ± 2.41 (200)	$p < 0.0001$	7.16 kg ± 3.58 (461)	$p < 0.0001$	5.66 kg ± 2.96 (315)	$p < 0.0001$
FTS-APC	9.88 kg ± 3.27 (296)		10.85 kg ± 2.81 (295)		10.64 kg ± 4.52 (207)	
Total	8.56 kg ± 2.95 (496)		8.60 kg ± 3.56 (756)		7.63 kg ± 4.37 (522)	
	Mean excess weight loss (*n*)		Mean excess weight loss (*n*)		Mean excess weight loss (*n*)	
FTS	17.95% ± 7.38 (202)	$p < 0.0001$	19.50% ± 9.95 (323)	$p < 0.0001$	11.30% ± 5.86% (272)	$p < 0.0001$
FTS-APC	25.11% ± 12 (216)		28.58% ± 12.12 (278)		25.05% ± 14.43 (191)	
Total	21.65% ± 9.34 (418)		23.74% ± 12.39 (601)		16.97% ± 11.19 (463)	
	Mean total body weight loss (*n*)		Mean total body weight loss (*n*)		Mean total body weight loss (*n*)	
FTS	5.75% ± 2.58 (130)	$p < 0.0001$	6.12% ± 4.14 (220)	$p < 0.0001$	4.09% ± 2.80 (200)	$p < 0.0001$
FTS-APC	8.38% ± 2.72 (216)		10.07% ± 3.38 (219)		10.61% ± 6.36 (132)	
Total	7.39% ± 2.64 (346)		8.09% ± 3.99 (439)		6.68% ± 5.09 (332)	
	Mean absolute weight loss (*n*)		Mean absolute weight loss (*n*)		Mean absolute weight loss (*n*)	
Superficial thickness	3.07 ± 3.81 (72)		4.44 ± 0.07 (102)		3.72 ± 7.42 (64)	
	Mean absolute weight loss (*n*)		Mean absolute weight loss (*n*)		Mean absolute weight loss (*n*)	
APC	15.48 ± 2 (30)		15.47 ± 9.12 (40)		No data	
	BMI at short-term × baseline BMI				BMI at long-term × baseline BMI	
OTSC	29.7 ± 1.8 × 32.8 ± 1.9	$p < 0.0001$			27.4 ± 3.8 × 32.8 ± 1.9	$p < 0.0001$

Table 2 Summary of included studies

FTS-APC	Country	Device	Baseline weight (kg)	Baseline BMI (kg/m^2)	Weight regain since nadir	Diet intervention/time	Comorbidities	Additional endoscopic therapy	*N*	Follow-up (months)
Kumar N 2016 [33]	USA	Apollo Overstitch	110.7	40.1	49.7%	Yes/8 weeks	NR	None	150	12
Gitelis M 2015 [38]	USA	Apollo Overstitch	115.2	42.2	23.4 kg	Yes/6 weeks	Some improvement	None	25	12
Kumar N 2014 [12]	USA	Apollo Overstitch	NR	41.1	40.9%/18.6 kg	Yes/6 weeks	23.7% improved DM	None	59	12
Total									234	
FTS	Country	Device	Baseline weight (kg)	Baseline BMI (kg/m^2)	Weight regain since nadir	Diet intervention/time	Comorbidities	Additional endoscopic therapy	*N*	
Goyal V 2013 [41]	USA	StomaphyX FT	96.6	36.1	16.2 kg	Yes/1 week	NR	None	59	41 ± 6
Thompson C 2012 [42]	USA	IOS USGI Medical	110.5	39.9	25.1 kg	Yes/NR	NR	None	116	12
Raman S 2011 [43]	USA	IOS USGI Medical	91	33.4	15.1 kg	Yes/NR	NR	None	37	4.69
Leitman I 2010 [46]	USA	StomaphyX FT	NR	39.5	NR	Yes/1 week	GERD improvement	None	64	5.8
Mikami D 2010 [44]	USA	StomaphyX FT	108	39.8	25.3 kg	Yes/2 weeks	GERD and diarrhea improvement	None	39	12
Horgan S 2010 [45]	USA	IOS USGI Medical	110.8	39.9	NR	Yes/NR	NR	None	116	6
Patel L 2016 [34]	USA	Full-thickness device	NR	41.3	23.76 kg	NR	NR	None	48	12
Gitelis M 2015 without APC [39]	USA	Apollo Overstitch	NR	41.6	24.8 kg	NR	GERD, OSA, hyperlipidemia, hypertension improvement	None	35	12
Kumar N 2014 without APC [40]	USA	Apollo Overstitch	NR	40.6	43%	NR	NR	None	84	12
Vargas E 2016 [35]	USA	Apollo Overstitch	NR	40.5	27.8 kg	NR	NR	None	29	12
Schulman A 2016 with ESD [36]	USA	Full-thickness device	NR	36.6	NR	NR	NR	ESD prior to suture	11	6
Schulman A 2016 [46]	USA	Full-thickness device	NR	39.8	NR	NR	NR	None	10	6
Total									648	

NR not reported, *GERD* gastroesophageal reflux disease, *OSA* obstructive sleep apnea, *AWL* absolute weight loss, *TBWL* total body weight loss, *EWL* excess weight loss

For the study [15] that assessed the efficacy of OTSC at treating weight regain, a total of 94 patients were included in the study with an average BMI of 32.8 ± 1.9 kg/m^2. This study only assessed BMI reduction as a measure of efficacy of this endoscopic technique. At 3 and 12 months, the mean BMI were 29.7 ± 1.8 and 27.4 ± 3.8 kg/m^2, respectively.

Results from qualitative analysis are summarized in Table 1.

Part II: Quantitative Analysis

Given a few number of studies that reported the efficacy of ST endoscopic suturing, APC, and OTSC at treating weight regain, only studies that evaluated FT endoscopic suturing were included in the quantitative analysis. Of the 26 studies that described FT endoscopic suturing, 15 studies with a total of 882 patients reported the mean with standard deviation or standard error and therefore were included in the final meta-analysis [12, 33–46]. Details of the included studies and their risk of bias and quality assessment are shown in Tables 2, 3, and 4, respectively. Average age and BMI were 50.8 ± 1.54 years and 40.2 ± 1.37 kg/m^2 at the time of FT endoscopic suturing. Only seven studies with 292 patients reported the amount of weight regain from nadir weight in kilograms with standard deviation. The average amount of weight regain was 18.6 ± 3.2 kg at the time of endoscopic suturing.

Short-Term Efficacy (0–3 months)

– Eight studies with a total of 320 patients reported short-term efficacy of FT-endoscopic suturing at treating weight regain. Average time of follow-up was 2.8 ± 0.7 months. Patients lost an average of 8.9 ± 0.71 kg, which represented 24.7 ± 2.5% of EWL at follow-up. A subgroup analysis including 221 patients in the FTS-APC group and 99 in the FTS-alone group demonstrated that the association of methods resulted in greater weight loss (9.0 ± 0.59 versus 5.5 ± 3.96 kg; 25.0 ± 1.99 versus 15.3 ± 9.88%, respectively) ($p < 0.001$) (Fig. 2a, b).

Mid-term Efficacy (3 < 12 months)

– Fourteen studies with a total of 619 patients reported mid-term efficacy of FT-endoscopic suturing. At 5.9 ± 0.35 months, the amount of weight loss was 10.3 ± 1.2 kg, representing 26.6 ± 4.15% EWL. Compared to FTS alone (405 patients), FTS-APC (214 patients) resulted in greater weight loss at the time of mid-term follow-up (10.6 ± 0.83 versus 9.4 ± 2.0 kg; 27.0 ± 2.91 versus 17.8 ± 15.3% EWL, respectively) ($p < 0.001$) (Fig. 2c, d).

Long-Term Efficacy (12 Months or Greater)

– Ten studies with a total of 455 patients reported long-term efficacy of FT-endoscopic suturing. At 15.3 ± 9.1 months, patients lost 9.8 ± 1.92 kg, which corresponded to 24.0 ± 4.38% EWL from baseline weight. The 173 patients in the FTS-APC group presented greater long-term weight loss compared to the remainder in the FTS-alone group (10.3 ± 1.42 versus 8.5 ± 2.98 kg, 24.2 ± 0.84 versus 11.7 ± 21.6% EWL, respectively) ($p < 0.001$) (Fig. 2e, f).

Graphs with trend lines of AWL and EWL through time are presented in Figs. 3 and 4. The blue lines represent the total result (FTS and FTS-APC) while the other two lines represent the results of each subgroup individually.

Table 3 Risk of bias of the studies included in the meta-analysis

Joanna Briggs Institute critical appraisal checklist for case series	Yes	No	Unclear
1. Were there clear criteria for inclusion in the case series?	5 (33.3%)	2 (13.3%)	8 (53.3%)
2. Was the condition measured in a standard, reliable way for all participants included in the case series?	13 (86.6%)	2 (13.3%)	
3. Were valid methods used for identification of the condition for all participants included in the case series?	12 (80%)	2 (13.3%)	1 (6.6%)
4. Did the case series have consecutive inclusion of participants?	12 (80%)	2 (13.3%)	1 (6.6%)
5. Did the case series have complete inclusion of participants?	5 (33.3%)	8 (53.3%)	2 (13.3%)
6. Was there clear reporting of the demographics of the participants in the study?	9 (60%)	2 (13.3%)	4 (26.6%)
7. Was there clear reporting of clinical information of the participants?	6 (40%)	6 (40%)	3 (20%)
8. Were the outcomes or follow-up results of cases clearly reported?	15 (100%)		
9. Was there clear reporting of the presenting site(s)/clinic(s) demographic information?	12 (80%)	2 (13.3%)	1 (6.6%)
10. Was statistical analysis appropriate?	15 (100%)		
Total (%)	69.3%	17.3%	13.3%%

Table 4 Summary of outcomes of the studies included in the meta-analysis

	Short-term AWL (kg)	Short-term TBWL (%)	Short-term EWL (%)	*N*	Mid-term AWL (kg)	Mid-term TBWL (%)	Mid-term EWL (%)	*N*	Long-term AWL (kg)	Long-term TBWL (%)	Long-term EWL (%)	*N*
FTS-APC												
Kumar N 2016 [33]	8.7	8.7	25.0	146	10.6	9.6	28.8	144	10.5	9.5	24.9	109
Gitelis M 2015 [38]	7	6.0	15.4	16	5.6	4.6	12.4	11	7.5	6.3	17.1	5
Kumar N 2014 [12]	14.2			59	10.6		20.4	59	8.6		18.9	59
Total				221				214				173
FTS												
Goyal V 2013 [41]	3.7		11.6	31	3.8		11.5	10	1.7		4.3	53
Thompson C 2012 [42]		2							5.5	5	14	73
Raman S 2011 [43]					4.2	4.7	23.5	37				
Leitman I 2010 [46]					7.3			64				
Mikami D 2010 [44]	6.7		13.1	15	8.7		17.0	14	10.0		19.5	6
Horgan S 2010 [45]					6.5		18	96				
Patel L 2016 [34]	7.3		17.4	32	5.6		14.7	28	4.2		8.3	18
Gitelis M 2015 without APC [39]							14.4	35			7.0	35
Kumar N 2014 without APC [40]					9.7			84	8.8			84
Vargas E 2016 [35]					8.8			16	8.8			13
Schulman A 2016 with ESD [36]	7.2		17.9	11	9.3		22.6	11				
Schulman A 2016 [46]	10.8		20.1	10	12.3		26.1	10				
Total				99				405				282

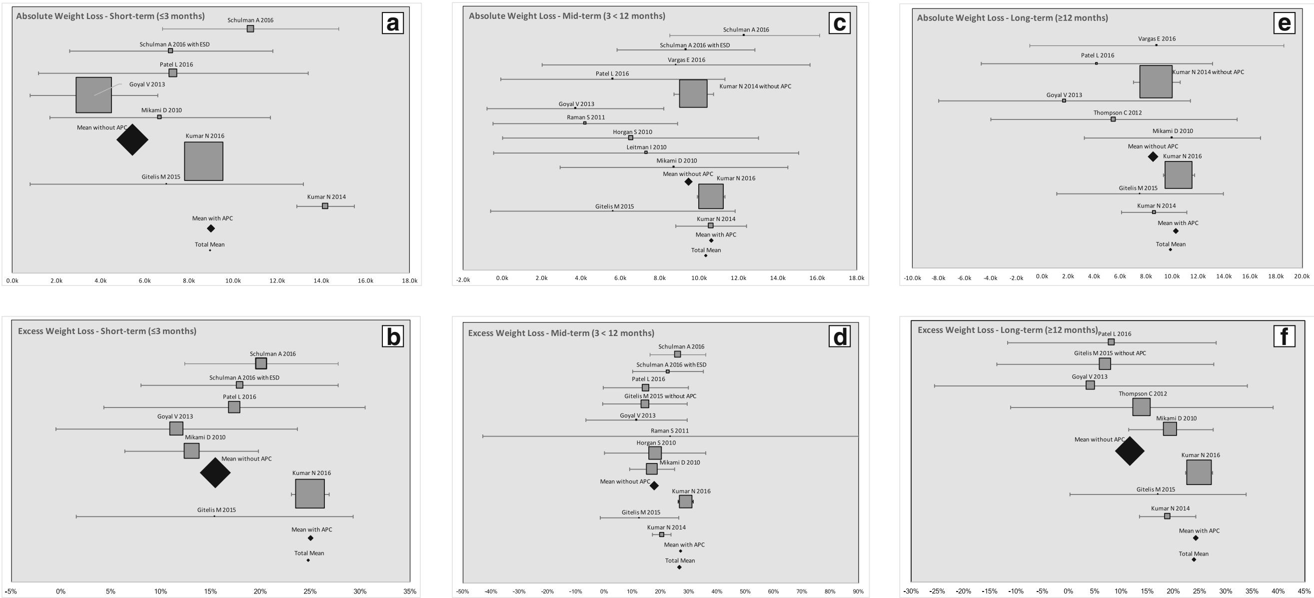


Fig. 2 Forest plots of the amounts of weight loss following full-thickness endoscopic suturing to treat weight regain at different follow-up time points. Subgroup analyses of the endoscopic suturing procedure with and without argon plasma coagulation (APC) show that endoscopic suturing with APC results in greater amount of weight loss than endoscopic suturing alone at all time points

Fig. 3 Mean absolute weight loss after full-thickness endoscopic suturing to treat weight regain

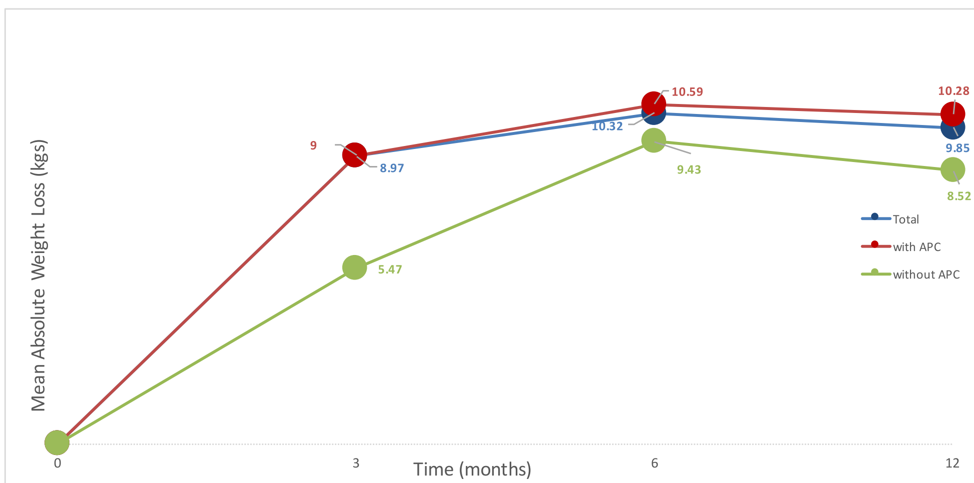
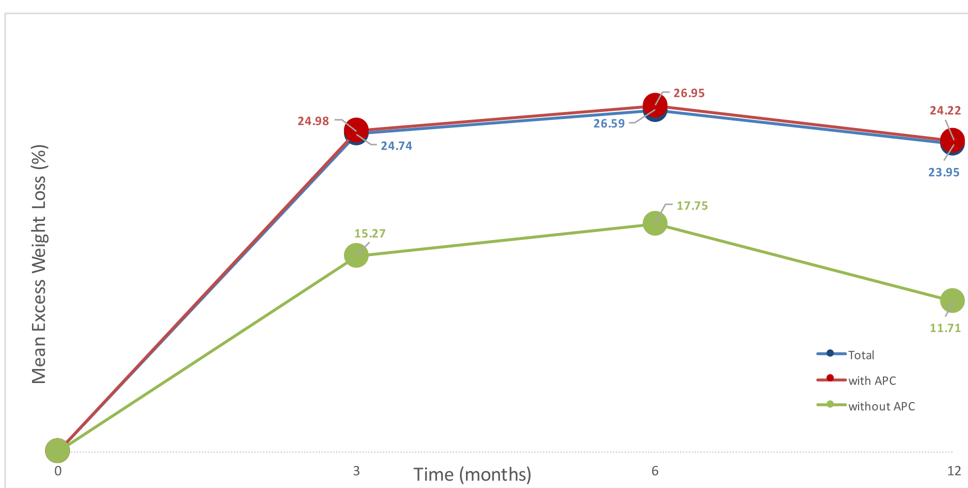


Fig. 4 Mean excess weight loss after full-thickness endoscopic suturing to treat weight regain



Discussion

This is the first systematic review and meta-analysis assessing the efficacy of endoscopic treatment for weight regain following RYGB. Our study demonstrates that transoral outlet reduction using full-thickness endoscopic suturing appears to be effective at treating weight regain with over 20% EWL at one year. Additionally, combining APC with endoscopic suturing results in greater weight loss than endoscopic suturing alone (Figs. 3 and 4).

Obesity is a rapidly growing pandemic [1]. In the USA, more than one third of the adult population was obese as of 2014, with an expected rise in the prevalence of obesity to 40% by 2030 [50, 51]. In addition to physical appearance, obesity is associated with multiple comorbidities including hypertension, hyperlipidemia, diabetes, and cardiovascular diseases that are leading causes of death worldwide [52].

Traditionally, the treatment options for obesity include lifestyle modification and bariatric surgery when lifestyle modification fails. Indications for bariatric surgery have historically been class II obesity (BMI $\geq$ 35 kg/m^2) with comorbidities and class III obesity (BMI $\geq$ 40 kg/m^2) [2]. However, more recently, it has been proposed that bariatric surgeries be performed on patients with class I obesity (BMI $\geq$ 30 kg/m^2) with metabolic comorbidities [53, 54].

With a rise in the number of bariatric surgeries being performed, gastroenterologists will continue to experience an increasing number of patients with suboptimal outcomes from bariatric surgery. Of these, weight regain is one of the most worrisome endings of RYGB. Specifically, it has been reported that up to 87% experience weight regain depending on the criteria used in definition [55], and up to about a third of patients regained almost all of the weight they had lost [42, 56]. Traditionally, treatment of weight regain involves revisional surgery, which itself carries short-term and long-term complication rates of 11.5 and 15.5%, respectively. Moreover, it has been reported that 13% of revisional surgery requires an additional surgical intervention with an even higher serious adverse event rate [11].

Given the complications associated with revisional surgery, transoral outlet reduction (TORe) has recently emerged as an alternative option to treat weight regain. These procedures may be categorized into sclerotherapy, ablation, clipping, and suturing groups. Our systematic review demonstrated that available literature on TORe remained heterogeneous in study design, described techniques, and measured outcomes. Of the available literature, full-thickness suturing had the most evidence supporting its efficacy and therefore was the main focus of the meta-analysis.

Our study demonstrated that full-thickness suturing to reduce the GJA size was effective at treating weight regain. Specifically, our meta-analysis showed that the amount of weight loss was approximately 25% EWL, which was achieved at 6 months and appeared to maintain at 12 months. Recently, a joint task force between the American Society for Gastrointestinal Endoscopy (ASGE) and the American Society for Metabolic and Bariatric Surgery (ASMBS) has defined a threshold of at least 25% EWL for a new primary bariatric therapy [57]. Endoscopic revision for weight regain may not need to reach this threshold; however, our study showed that full-thickness endoscopic suturing was able to achieve it.

In addition, our study was also the first study to compare suturing TORe with APC to that without APC. As far as we know, there has been no previous report on this comparison likely due to the studies being underpowered. Our meta-analysis showed that performing APC around the gastrojejunal anastomotic rim prior to suturing resulted in greater weight loss than suturing alone at 3, 6, and 12 months. This was likely a result of deeper submucosal-to-submucosal tissue apposition achieved via APC, which likely led to more effective and durable weight outcome.

This study has some limitations. First, there have been no randomized controlled trials evaluating the efficacy of revisional procedure for weight regain with full-thickness endoscopic suturing. Therefore, our meta-analysis included only observational studies without a control arm to compare the results of the intervention arm with. This fact may have introduced some bias and heterogeneity regarding patients' baseline characteristics. Moreover, the quality of evidence of the included studies was very low, which also impairs firm conclusions. However, by pooling the data from all available articles, we were able to include a large number of patients and studies, which helped amplify generalizability and reduce the impact of sampling bias. Secondly, our study compared the efficacy of FTS with and without APC, although there currently has been no existing study that compared these two procedures head to head. We were able to perform this comparison using the pooled data. However, biases may have arisen due to differences in patients' baseline characteristics and follow-up strategies.

In conclusion, our study shows that full-thickness suturing to reduce the gastrojejunal anastomotic size is effective at treating weight regain after RYGB. Performing APC prior to suturing seems to result in greater weight loss compared to suturing alone. Head-to-head studies are needed to confirm our results. Additionally, a comparison study to evaluate the cost and benefit ratio of FTS-APC and surgical revision will provide further insight into the optimal care for this challenging patient population. For now, few studies adequately assess effectiveness of other endoscopic techniques.

Compliance with Ethical Standards

Conflict of Interest Dr. Galvao Neto reports personal fees from Apollo Endosurgery, Fractyl Labs, GI Windows, GI Dynamics, Ethicom Endosurgery, and Alacer Biomedica outside the submitted work. All other authors have nothing to declare.

Ethical Approval Statement All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Statement Informed consent does not apply for this study.

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