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Efficacy of the argon plasma coagulation in patients with weight regain after gastric bypass: a randomized control trial

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ABSTRACT

Background and study aims Endoscopic procedure using argon plasma coagulation (APC) promotes a progressive reduction in gastrojejunal anastomosis diameter. The present study aimed to evaluate the efficacy of the APC in patients with weight regain in the postoperative periods of gastric bypass.

Patients and methods This was a randomized controlled trial conducted with 66 patients who were randomly assigned selected (using lottery method) and divided into two groups: study group (SG), 38 patients (APC treatment); and control group (CG), 28 patients (only endoscopy procedure). We considered 30 days,180 days, and one year as short-term, medium-term, and long-term, respectively. The parameters analyzed were total weight loss (TWL), excess weight loss (%EWL), total weight loss (%TWL), and reduction of weight regain (%RWR). Furthermore, a biopsy for neoplastic histological changes was carried out for the APC group. For statistical analysis, values of $P<0.05$ were considered significant.

Results The %TWL and %RWR were higher in the SG in short, medium, and long terms, when compared to the same periods in the CG ($P<0.001$). One year after follow-up, the final weight did not reach the statistical difference between groups. Biopsy performed in SG 1 year after APC did not reveal neoplastic histological changes.

Conclusions APC effectively treats weight regain after bariatric surgery in the short and medium-term. An important "new" weight gain was observed in the long-term, showing that obesity is a chronic disease that requires multidisciplinary and family care for life. Also, APC is a safe procedure with low adverse event rates.

Introduction

Roux-en-Y gastric bypass (RYGB) has shown satisfactory short-term results, such as a significant reduction in body weight and modification of intestinal hormones involved in appetite signaling glycemic control [1]. RYGB is also highly effective for long-term excess weight loss (EWL), ranging from 51 % to 83 % [2]. However, the long-term follow-up also indicated that 10 % to 20 % of the patients regained weight, and several methods

have been proposed to minimize the weight regain [3]. Endoscopic procedures targeting reduction in the diameter of the gastric pouch or gastrojejunal anastomoses, such as endoluminal injection of sodium morrhuate [4], Endocinch [5], Stomaphyx [6], ROSE procedure [7], Overstitch of Apollo Endosurgery [8], OTSC clip [9], and argon fulguration of gastrojejunal anastomosis [10], have been reported in the literature to minimize post-bariatric significant weight regain.

Argon is an odorless, inert, non-toxic, inexpensive, and easily ionizable gas that has been used in conventional surgeries since the 1980 s and was introduced in the field of endoscopy in 1991 [11]. Argon fulguration is a noncontact electrocoagulation method in which radiofrequency energy is applied to the tissue using ionized argon gas via an electric current, defined as plasma [12]. The penetration depth is between 1 and 3 mm, although some studies show clearly that the higher the intensity, the greater the depth of the lesion, eventually reaching the submucosa [13].

In gastrojejunal anastomosis, argon plasma coagulation (APC) promotes a progressive reduction in its diameter, leading to a "stenosis" that delays gastric emptying and promotes early satiety, which could result in weight reduction [12]. In recent years, endoscopic techniques have been implemented, aiming at efficiency and low risks to patients. However, few prospective studies with bias control were performed concerning the treatment of weight regain after bariatric surgery, with most case reports [13]. This fact was documented in a meta-analysis [14], proving the effectiveness of anastomosis treatment in patients with weight regain after RYGB, with the treatment of endoluminal suture and suture associated with argon plasma ablation. However, isolated studies of APC are scarce, so its effectiveness cannot yet be scientifically proven. The Federal Council of Medicine in Brazil still does not recommend carrying out this procedure to treat weight relapse (Opinion No. 39/16), outside research protocols, due to the scarcity of scientific studies proving its efficiency and safety [15].

Considering the positive reports about APC utilization, this study aimed to evaluate its efficacy in patients with weight regain after bariatric surgery in the short-, medium-, and long-term postoperative periods.

Patients and methods

Study design and population

This was a 1-year follow-up to a randomized controlled trial (RTC). The single-blinded approach of this study was intended to ensure that the control group, which was not submitted to APC, would not have the placebo effect. Only the physician responsible for the procedures knew which patients were part of the study and control groups.

The exclusion criteria were: patients younger than 18 years; those who did not accept or could not perform the endoscopy exam and follow-up during the study; abandoned the study before the third assessment; patients with a history of recent neoplasia (after bariatric surgery), with reoperation of bariatric surgery, with immediate or late postoperative adverse events (AEs) that required further surgery; patients who underwent other surgical techniques; and have a gastrojejunal anastomosis smaller than 1.2 cm in its largest measurement axis. All participants underwent a previous endoscopy, the steps of which are described in the section "endoscopic evaluation."

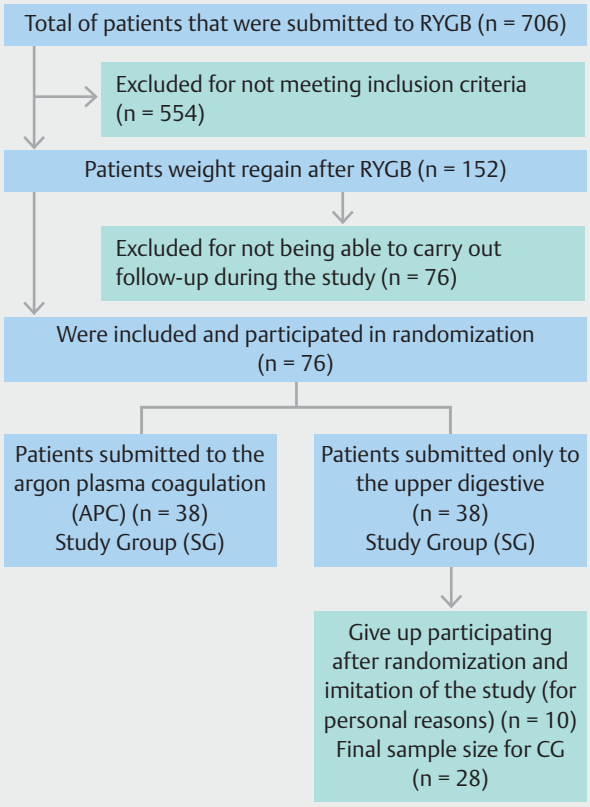
At the beginning of the study, 706 medical records of patients that were submitted to RYGB (without placing the Silastic ring) at the Hospital de Base of São José do Rio Preto Medical School (HB/FAMERP) from June 2010 to June 2016 were evaluated. Among them, 152 patients were identified with weight regain higher than 10 % of the minimum weight reached 24 months after RYGB. Of the 152 patients, 76 (50 %) were excluded because they matched one or more exclusion criteria previously described. Thus, 76 patients (50 %) were selected, included, and allocated into two groups (using the random assign /lottery method): study group (SG), composed of 38 patients (50 %), submitted to upper digestive endoscopy (UDE) for application of APC and control group (CG), composed of 38 patients (50 %) who underwent UDE but not APC. Of the total number of participants in the CG, 10 (13 %) withdrew from the study for personal reasons. Thus, 66 individuals were included in the study (▶ **Fig. 1**). In the lottery method, the physician responsible for the procedures placed all numbers individually in a bucket and drew numbers at random for each group.

The manuscript was prepared following the CONSORT stands for Consolidated Standards of Reporting Trials and the protocol was approved by the Ethics Committee of the São José do Rio Preto Medical School (CAAE: 65678117.7.0000.5415) and registered in https://ensaiosclinicos.gov.br/rg/RBR-10jyygyg (The Universal Trial Number – UTN is U1111-1259-6021 and approval number: RBR-10jyygyg). The study was performed according to the World Medical Association's Declaration of Helsinki guidelines.

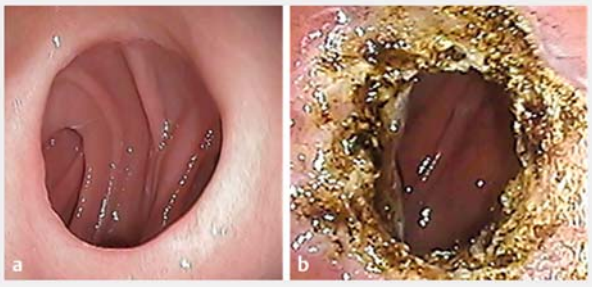
Endoscopic evaluation

Patients fasted for 8 hours, were positioned in left lateral decubitus, and received an instillation of 10 % of topical xylocaine spray and 50 mcg of fentanyl by intravenous injection (IV), midazolam 5 mg IV, and propofol at the IV criterion with adequate cardiopulmonary monitoring throughout the exam. After sedation, UDE was performed with a Pentax endoscope (Pentax, Tokyo, Japan). For analysis and to measure the largest and smallest dimension of anastomosis elliptical shape, biopsy forceps with a 0.7-cm reference were used. The largest measurement for data analysis was considered.

Subsequently, the SG patients were submitted to APC (WEM SS200E, Ribeirao Preto, SP) with a disposable endoscopic catheter in gastrojejunal anastomosis from 1.2 cm. An 80 W power and 1.0 L/min flow were used across the circumference, extending for about 2.0 cm from the gastric pouch, molding the region to the endoscopic device (9.8 mm) (▶ **Fig. 2a**, ▶ **Fig. 2b**). The procedure ended when resistance to the device was observed in the gastrojejunal anastomosis. Although the importance of anatomical restriction, the ideal measure of anastomosis, is still controversial, in this instance, the literature suggests a range between 1.2 cm and 2.0 cm [16]. The minimum diameter was



▶ **Fig. 1** Flowchart of group selection and steps of the study. Were evaluated 706 medical records of patients that were submitted to the Roux-en-Y gastric bypass (RYGB). Of this total, 554 did not meet the inclusion criteria. Then 152 patients were identified with weight regain higher than 10 % of the minimum weight reached 24 months after the RYGB. Of the 152 patients, 76 (50 %) were excluded because they matched one or more exclusion criteria. Thus, 76 patients (50 %) were selected, included, and allocated into two groups (using the random assign /lottery method): study group (SG), composed of 38 (50 %) patients, submitted to the upper digestive endoscopy (UDE) for the application of APC and control gGroup (CG), composed of 38 (50 %) patients who underwent the UDE but not to the APC. Of the total number of participants in the CG, 10 (13 %) gave up participating for personal reasons.



▶ **Fig. 2** Illustrative photograph of the dilated gastrojejunal anastomosis region. **a** Anastomosis before applying the argon plasma coagulation. **b** Tissue after applying argon plasma coagulation.

1.2 cm in the present study, similar to that with manual gastrojejunal anastomosis.

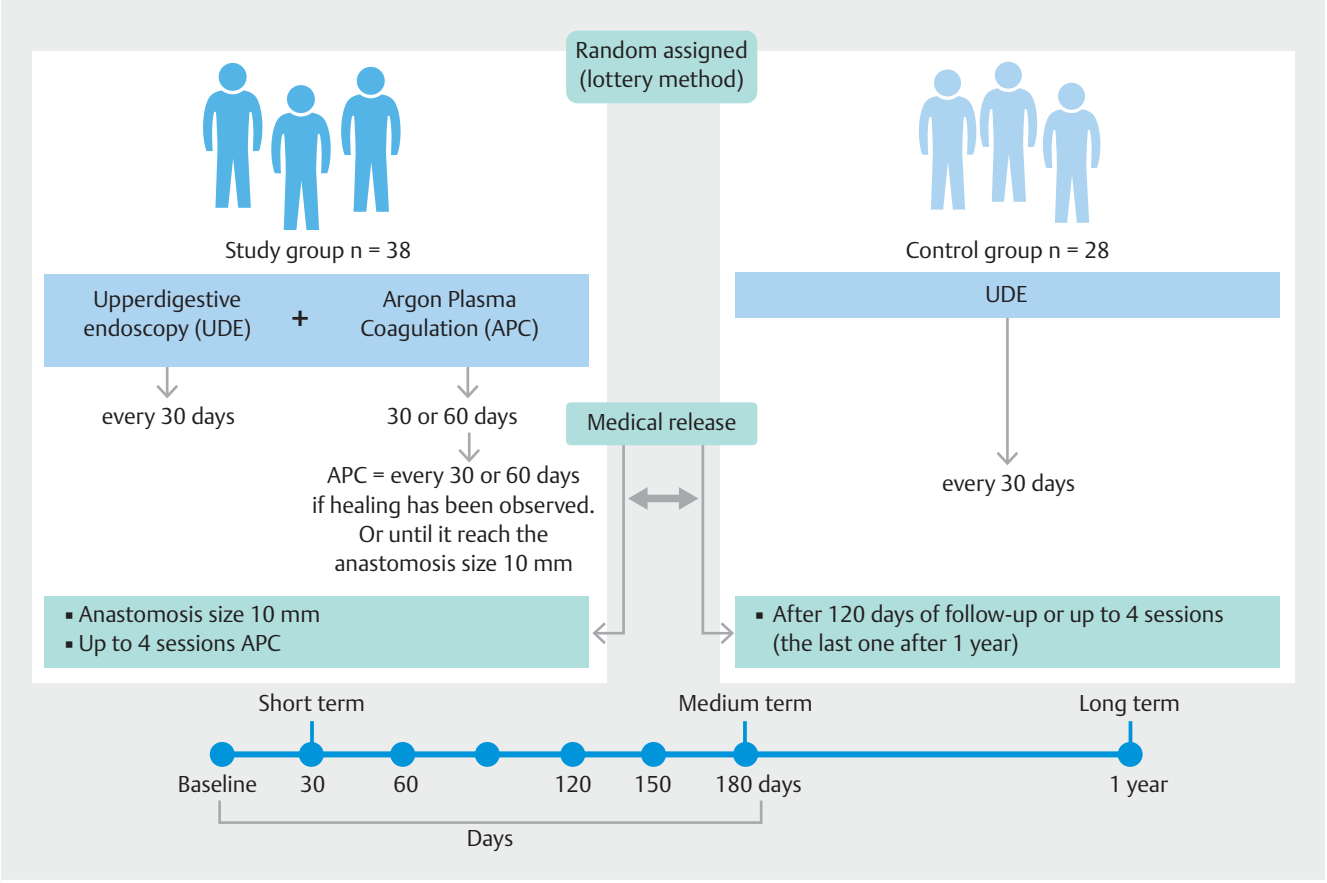
Patients were also submitted to endoscopic examination without application of APC as a control group, to avoid measurement errors related to regression to the mean and differential misclassification bias. Both groups underwent identical amounts and periods of endoscopy. The only difference between the groups was application of APC performed in the SG. Endoscopic evaluation was performed in the Endoscopy Service of HB/FAMERP every 4 weeks, and APC was performed at intervals of 4 to 8 weeks, depending on the healing process and anastomosis size, for up to four sessions. The APC procedure schedule included visits at 30, 60, 90, 120, 150, 180 days, and 1 year. Thirty days after the first visit was considered short-term. The medium-term period was up to 180 days, and the long-term period was 1 year after the beginning of group monitoring (▶ **Fig. 3**).

Medical release for patients who underwent APC was determined by measuring the anastomotic diameter when its minimum value of 10 mm was reached. Lower values could contribute to weight regain. The second indication for medical release was determined by the number of procedures performed, with up to four APC sessions indicated. Medical release was determined for the CG after 120 days of follow-up. One year after APC, patients underwent repeat UDE to assess the gastrojejunal anastomosis previously modified with the procedure (▶ **Fig. 3**). A biopsy was performed locally to verify the absence/presence of neoplastic factors in the region cauterized by APC. Maintenance of lost weight also was evaluated.

Demographic, clinical, operative, and endoscopic evaluations

We analyzed: 1) demographic data: gender and age; 2) anthropometric and clinical data: height, weight, body mass index (BMI), excessive weight (difference between pre-surgery weight and ideal weight), weight regain (difference between the weight of the evaluated postoperative period and the lowest weight achieved during the postoperative period), and time after gastric bypass); 3) operative: AEs after laparoscopic gastric bypass; and 4) endoscopic (diameter of anastomosis in each APC session) evaluations. Weight was measured using a Filizola platform with a digital scale, with a capacity of 300 kg and a precision of 0.2 kg. To measure height, we used a vertical stem with 0.5-cm graduation. BMI was obtained using BMI = weight/height^2, weight in kilograms, and height in meters. Patients were considered to have regained weight if they gained more than 10 % of the total weight loss after the second year of bariatric surgery.

Five measures were used to assess weight loss: total weight loss (TWL = pre-procedure weight minus actual weight), percentage of EWL (%EWL), percentage of total weight loss (% TWL), percentage reduction of regained weight (%RWR), and BMI. TWL was calculated by the absolute weight loss expressed in kilograms. %EWL considered the percentage of weight loss compared with excess weight, defined as current weight minus the weight corresponding to a BMI of 25 kg/m^2 (weight loss/excess weight). %TWL was calculated using the absolute weight



▶ **Fig. 3** Study design. This study comprised 1 year of follow-up, which was performed according to the general clinical status of each patient at 30, 60, 90, 120, 150, 180 days, and 1 year for both groups: study group (SG) submitted to the upper digestive endoscopy (UDE) for the application of APC and control group (CG). Short-term, medium-term, and long-term follow-ups were defined as 30, 180 days, and 1 year of follow-up, respectively. For the SG, if the patient did not present healing or had already reached a 10-mm anastomosis shown during endoscopy, the application of argon plasma coagulation (APC) was not performed. A medical release was defined by the same number of sessions (up to 4) or until the SG reached 10 mm of anastomosis size.

loss percentage above patient total weight pre-procedure (weight lost/pre-procedure weight), and the %RWR is the reduction of the regained weight expressed in percentage (weight lost/regained weight).

After endoscopy with or without APC, both groups were instructed to maintain a restrictive diet to avoid discomfort or other unpleasant symptoms. At the same time, all participants were encouraged to carry out multidisciplinary follow-up, including consultations with psychologists, nutritionists, and physical activity practice. In addition, they were instructed to keep in touch with a doctor to report any signs or symptoms different from the usual. However, due to the dynamics of the service and patient compliance, follow-up with the multidisciplinary team was not controlled.

Statistical analysis

The Kolmogorov-Smirnov test was used to assess normality of data distribution. Descriptive statistics values were presented as mean and standard deviation. Linear mixed models for repeated measures were performed to compare groups and times regarding weight, BMI, %EWL, %TWL, TWL, and %RWR. A student's *t*-test was proposed to compare the groups regarding weight regained after surgery. Spearman's correlation coefficient and multiple linear regression were used to verify correlations between each group's clinical, demographic, operative, and endoscopic variables. Power calculation was performed using the software Origin 2016 and considering parameters of weight regain after APC from the previous studies [12]. For a desired power of 80 % and a significance of 0.05, the calculated sample size required was 26. Two-sided $P < 0.05$ was considered statistically significant. All calculations were performed with R software version 4.0.4, SAS 9.4, and Statistical Package for Social Science software (SPSS version 20.0, Inc. Chicago, Illinois, United States).

Results

Demographic, clinical, operative, and anthropometric data

A total of 76 patients were initially screened for inclusion in this study, divided into two groups, n = 38 (SG) who received the APC and n = 38 (CG) who underwent endoscopy but did not re-

▶ **Table 1** Demographic and anthropometric profile of patients submitted to gastric bypass technique with Roux-en-Y reconstruction, without placing the Silastic ring[1]

	Study group (n = 38)	Control group (n = 28)	*P* value
Variable	**M ± SD**	**M ± SD**	
Age (years)	45 ± 8.5	42 ± 9.1	0.193
95 % CI	(42.1–47.8)	(38.5–45.8)	
Sex			
Women (n/%)	33/86.8	26/92.8	0.175
Men (n/%)	5/13.2	2/7.2	
Anthropometric profile			
Weight (kg)	98.5 ± 21.2	95.6 ± 15.7	0.448
95 % CI	(92.4–104.6)	(88.5–102.7)	
BMI (kg/m²)	37.5 ± 6.3	36.3 ± 6.2	0.241
95 % CI	(35.5–39.5)	(33.9–38.6)	
Maximum Weight Loss after RYGB	40.1 ± 11.4	42.2 ± 12.4	0.030
95 % CI	(38.1–43.2)	(38.7–46.2)	
Excessive weight (kg)	33.1 ± 18.0	29.5 ± 15.6	0.364
95 % CI	(28.7–36.1)	(25.9–32.1)	
Weight regains (%)	33.7 ± 0.1	31.0 ± 0.1	0.392
95 % CI	(30.0–37.1)	(27.2–35.0)	

M, mean; SD, standard deviation; BMI, body mass index; RYGB, gastric bypass with Roux-en-Y; 95 % CI, confidence interval; APC, argon plasma coagulation. Excessive weight is the difference between pre-surgery weight and ideal weight. Weight regain is the difference between the weight of the evaluated postoperative period and the lowest weight achieved during the postoperative period.
[1] With the application of argon plasma coagulation (APC) (study groups) or without APC (control group) in the pre-intervention period (baseline).

ceive APC. Of the total number of participants in the CG, 10 (13 %) withdrew from the study for personal reasons. Thus, 66 individuals were included in the study (▶ **Fig. 1**). Patients were selected for this study from January 2018 to January 2020. The trial was completed in 2020 due to the COVID-19 pandemic and for having already reached a sufficient sample size, as the calculation suggested. Both groups were similar in age, sex, weight, BMI, excessive weight, and postoperative weight regain (▶ **Table 1**). ▶ **Table 2** presents the analysis of weight, BMI, TWL, %EWL, %TWL, and %RWR in different periods, intragroup and between groups. We found a significant difference in TWL, % EWL, %TWL, and weight regain between CG and SG ($P < 0.05$) in all periods. The period of time between postoperative RYGB and beginning of APC did not differ between groups (SG = 29.5 ± 5 and 30.2 ± 2 months for CG) ($P > 0.05$).

In the short-term 37 patients (97.3 %) in the SG lost weight (max = 11 kg; min = 1 kg), reaching TWL of 4.8 ± 2.7 kg, %EWL of 22.8 ± 33.7 % (95 % IC: 14.8–30.8), %TWL of 4.8 ± 2.4 % (95 % CI: 3.5–6.1), and %RWR of 46.5 ± 34.4 % (95 % IC: 31.9–61.0). During the same period in the CG, 19 patients (67.8 %) lost weight (max = 6 kg; min = 1 kg), 3 (10.7 %) maintained initial weight, and 6 (21.4 %) gained weight (max = 2 kg). Thus, the mean value of TWL was 1.6 ± 2.0 kg, %PEP 9.3 ± 13.9 % (95 % IC: 0.0–18.6), %TWL 1.8 ± 2.2 % (95 % IC: 0.2–3.3), and %RWR 17.1 ± 21.0 % (95 % IC: 0.1–34.0). After medical release, in the medium-term, both groups maintained the differences for TWL, %EWL, %TWL, and %RWR ($P < 0.05$). In the long-term, we did not find differences in mean weight values between groups. The number of participants during follow-up remained unchanged at baseline, short-term, and medium-term for both groups (SG: n = 38 and CG: n = 28). However, we observed that 87 % (n = 33) of SG patients and 78.5 % (n = 22) of CG patients returned to complete the protocol during the 1-year follow-up evaluation.

Secondary outcomes

Gastrojejunal anastomosis

Endoscopic follow-up was performed every 30 days in all patients. After 4 weeks of APC, 78.9 % of patients in the SG had edema and ulcer, deforming the region and distorting anastomosis measurement. In these cases, new application of the APC was not performed until site recovery. ▶ **Fig. 4** illustrates the healing process in the 30 days, showing an ulcer in a regenerative process with hyperemia around it. At 60 days, three patients (7.8 %) had problems during the regenerative process, and 92.2 % were completely healed.

▶ **Table 2** Intra and between-groups analysis of study group and control Group with mean values (M) and standard deviations (SD) for weight, BMI, AWL, %EWL, %TWL, RWR in short-term, medium-term, and long term, in patients with weight regain.

	Study group (SG)				Control group (CG)			
Variable	**Baseline N = 38**	**30 days Short-term N = 38**	**180 days Medium-term N = 38**	**1-year Long-term N = 33**	**Baseline N = 28**	**30 days Short-term N = 28**	**180 days Medium-term N = 28**	**1 year Long-term N = 22**
	M ± SD	M ± SD	M ± SD	M ± SD	M ± SD	M ± SD	M ± SD	M ± SD
Weight	98.5 ± 21.2	93.7 ± 20.2[1]	81.3 ± 2.3[1,2]	94.2 ± 21.6[1,2,3]	95.6 ± 15.7	94.0 ± 16.0[4]	93.8 ± 15.8[4]	97.7 ± 15.1[5,6,7]
(95 % CI)	(92.4–104.6)	(87.6–99.8)	(75.1–87.2)	(87.5–28.0)	(88.5–102.7)	(86.9–01.1)	(86.7–100.0)	(90.0–104.2)
BMI (kg/m^2)	37.5 ± 6.3	35.7 ± 6.2[1]	31.1 ± 8.5[1,2]	36.2 ± 6.8[1,2,3]	36.3 ± 6.2	35.7 ± 7.1[4]	35.6 ± 6.2[4,5]	37.5 ± 6.0[5,6,7]
(95 % CI)	(35.5–39.5)	(33.7–37.7)	(25.2–37.4)	(30.3–42.2)	(33.9–38.6)	(33.3–38.0)	(33.3–38.0)	(34.5–39.2)
TWL (kg)	–	4.8 ± 2.7	7.4 ± 3.8[2]	1.5 ± 5.5[2,3]	–	1.6 ± 2.0[8]	1.7 ± 3.8[8]	1.7 ± 5.2[5,6,8,7]
(95 % CI)		(3.5–6.1)	(6.1–8.7)	(0.5–3.2)		(0.1–3.1)	(0.2–3.2)	(-3.1–0.1)
%EWL	–	22.8 ± 33.7	30.3 ± 25.5[2]	15.1 ± 61.3[2,3]	–	9.3 ± 13.9[8]	6.4 ± 18.5[8]	8.3 ± 18.7[5,6,8,7]
(95 % CI)		14.8–30.8	22.3–38.3	(-0.3–16.4)		(0.0–18.6)	(-2.8–15.7)	(-16,1–3.7)
%TWL	–	4.8 ± 2.4	7.5 ± 3.6[2]	1.8 ± 5.7[2,3]	–	1.8 ± 2.2[8]	1.8 ± 4.2[8]	1.9 ± 5.2[5,6,8,7]
(95 % CI)		(3.5–6.1)	(6.2–8.8)	(0.7–3.4)		(0.2–3.3)	(0.3–3.3)	(-3.3–0.0)
RWR (%)	–	46.5 ± 34.4	69.4 ± 47.8[2]	21.9 ± 62.9[2,3]	–	17.1 ± 21.0[8]	13.8 ± 38.9[8]	20.6 ± 54.9[8]
(95 % CI)		(31.9–61.0)	(54.9–83.9)	(6.1–36.8)		(0.1–34.0)	(-3.0–30.7)	–37.1–0.0)

Linear mixed models were applied.
SG, study group; CG, control group; BMI, body mass index; M, mean; SD, standard deviation; TWL, total weight loss; %EWL, excess weight loss; %TWL, total weight loss; RWR, reduction of weight regain; CI, confidence interval.
Significance level, $P < 0.05$
[1] When compared with baseline of SG.
[2] When compared with short-term of SG.
[3] When compared with medium-term of SG.
[4] When compared with baseline of CG.
[5] When compared with short-term of CG.
[6] When compared with medium-term of CG.
[7] When compared with long-term of SG.
[8] When study SG is compared with CG in the same period.

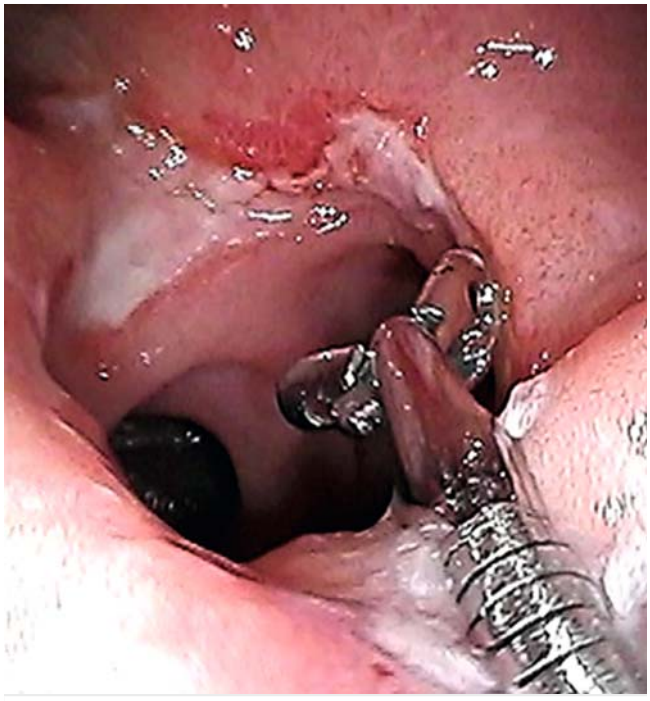
A reduction in gastrojejunal anastomosis diameter was statistically significant after the APC (short-term) compared with pre-procedure ($P < 0.05$). We also found statistically significant differences in the period between 60 and 90 days pre-procedure and 60 and 90 days, between 60 and 120 days pre-procedure and 120 days, and pre-procedure and 180 days ($P < 0.05$ for all these analyses). One year after the procedure (long-term), an increase in anastomosis was evident compared to the medium-term ($P < 0.05$). ▶ **Table 3** shows the mean values, standard deviations, median, minimum, and maximum of gastrojejunal anastomosis diameter for all evaluated periods. At the beginning of the study, the SG had a mean value of gastrojejunal anastomosis diameter of 3.82 ± 1.57 cm, with values from 2.04 (minimum) to 7.57 cm (maximum). At discharge (which varied according to response to APC reaching the recommended anastomosis size), the mean was 1.69 ± 0.36 cm, ranging from 1.27 to 3.08 cm.

When we investigated average values between the pretreatment period and after reaching the appropriate diameter, we observed values of 2.13 ± 1.55 cm, minimum values of –0.05 cm, and a maximum of 5.98 cm. We also observed that nine patients (27.27 %) had an increase in the diameter of the gastrojejunal anastomosis after 1 year.

In the multiple linear regression analysis, we considered the gastrojejunal anastomosis diameter as a dependent variable, and the independent variables were sex, BMI, weight, and age. We did not find significant differences in the models applied ($P > 0.05$). Therefore, the independent variables explained the dependent variable in values below 1 %. The Spearman test showed a positive correlation between age and the anastomotic mouth diameter after 90 days of the procedure (r = 0,554; $P < 0.05$). The other variables in this study, including anastomotic mouth diameter, age, sex, TWL (kg), %EWL, %TWL, and %RWR, did not show correlations.

APC adverse events

Considering the 38 patients (SG) undergoing the APC procedure, only one (2.6 %) had anastomosis stenosis. The APC procedure was not associated with intestinal perforation, bleeding, or any other type of anatomical AE.



▶ **Fig. 4** Gastrojejunal anastomosis ulcer in a patient submitted to Roux-en-Y gastric bypass technique without placing the Silastic ring after 30 days of argon plasma coagulation application.

Histological analysis of gastrojejunal anastomosis

Biopsy of the gastrojejunal anastomosis region 1e year after the procedure (long-term) indicated four histological patterns. Sixty-nine percent of patients in the SG and 60 % in the CG had chronic gastritis, 12.1 % in the SG had incomplete intestinal metaplasia with atrophy, 6 % in the SG had complete intestinal metaplasia with atrophy, 6 % in the SG and 20 % in the CG had complete intestinal metaplasia without atrophy, 3 % in SG and 5 % in the CG had incomplete intestinal metaplasia without atrophy, and 3.0 % in SG and 5.0 % in the CG had atrophy without metaplasia.

Discussion

The present study demonstrated the efficacy of APC in reducing the diameter of gastrojejunal anastomosis, leading to a reduction in anthropometric parameters of patients with weight regain after bariatric surgery, corroborating the literature in which APC reduces the diameter of gastrojejunal anastomosis with a consequent decrease in body weight over the short and medium terms [17, 18]. However, the main point of this study reveals that there is a "new weight regain" in the long term, showing that obesity is a chronic disease and that even after different interventions for weight loss, such as bariatric surgery and APC, patients still cannot stabilize their weight.

In the present study, after endoscopic interventions, 97.3 % of SG participants showed a reduction from initial weight in the medium-term, while we did not observe differences in the CG.

▶ **Table 3** Mean values and standard deviations for the gastrojejunal anastomosis diameter of patients undergoing APC (study group), including median, minimum and maximum values.

Gastrojejunal anastomosis diameter	Study Group		
	n	M ± SD	Median (min/max)
Pre APC	38	3.82 ± 1.57	3.38 (2.04/7.54)
30 days (short-term)	38	2.18 ± 1.13[1]	1.88 (1.13/6.28)
60 days	37	2.36 ± 1.1	2.04 (1.13/6.28)
90 days	22	1.89 ± 0.59[1,2]	1.73 (1.13/3.3)
120 days	14	1.9 ± 0.63[1,2]	1.63 (1.13/3.08)
150 days	6	2.26 ± 1.16	1.88 (1.41/4.54)
180 days (medium-term)	1	3.08[1]	3.08 (3.08/3.08)
210 days	1	3.08	3.08 (3.08/3.08)
1 year (long-term)	33	2.82 ± 1.36[2]	2.64 (1.41/6.59)
At discharge[3]	38	1.69 ± 0.36	1.57 (1.27/3.08)
Pre vs post-APC	38	2.13 ± 1.55	1.8 (-0.05/5.98)

Linear mixed models were applied; significance level for $P<0.05$.
SD, standard deviation.
[1] When compared with pre-application of argon plasma.
[2] When compared to 60 days after APC.
[3] Which varied according to the response to APC reaching the recommended size for the anastomosis.

TWL was higher in the SG compared to the CG for the same period. Baretta et al. [12] performed approximately three sessions of APC to reduce gastrojejunal anastomosis in 30 patients and observed an 89 % reduction in regained weight, with an average weight loss of 15.4 kg. De Souza et al. [19] evaluated 37 participants after two APC sessions and obtained a 24.0 % reduction in regained weight with a weight loss of 5.87 kg.

This study showed an increase in %TWL in the SG compared to the CG in the medium and long terms. These data were consistent with the Moon et al. [20] study that analyzed 558 patients undergoing APC in bariatric centers in Brazil and the United States, showing a %TWL of 6 to 10 % in 12 months. Recently, Grover et al. [21] analyzed variability in bariatric surgery results based on percentage of %TWL in a retrospective study with 1574 patients. They concluded that %TWL resulted in less variability when stratified by several preoperative characteristics of patients. Therefore, a standard metric should be considered to assess response, weight loss, and weight regain. Lack of global standardization for measuring ideal expression of the outcome related to weight loss hinders studies on the theme of weight regain, with variable rates in the literature depending on the definition, decreasing the quality of available evidence.

In the present study, participant weight was also analyzed after 1 year. The results were contrary to expectations, with a "new" weight regain observed in both groups, indicating that APC outcomes regarding weight loss could not be relied upon in the long term. Our results provide important and innovative data about the "new" weight regain, supporting the hypothesis of Marchesini et al. [22], in which APC alone would not be sufficient for weight loss and weight loss maintenance in the long term. Nonetheless, about the "new" weight regain after endoscopic procedures is limited and more studies should be conducted to further address the prevalence and mechanism involved.

The present study also analyzed anatomical AEs, such as stenosis, hemorrhage, and intestinal perforation. Of the 38 patients, only one had stenosis after cauterization of the gastrojejunal anastomosis. It occurred because of the 9.8-mm-gauge endoscopic device's inability to pass through the anastomosis (with a 5-mm diameter). This case was solved with three sessions of pneumatic dilation of the stenosed region, intending a diameter close to 10 mm, maintaining the partial local restriction and improving food tolerance.

In this study, there was no evidence of bleeding or intestinal perforation, possibly due to penetration of 1 to 3 mm of the APC, resulting from the loss of electrical conductivity in tissues cauterized by local dehydration. In this case, APC is redirected to another electrically conductive zone (low impedance zone), continuing the process until the entire anastomosis is treated. The literature reveals that AEs caused by this type of procedure are rare [20]. On the other hand, Zingg et al. [23] evaluated AEs from reoperation for weight regain treatment in 61 patients who underwent gastric bypass review. They showed higher rates of surgical AEs compared to the first surgery to treat obesity. Possible reasons that justify these differences were the fibrotic and inflamed tissue found during the second operation, tissue ischemia due to crossing several staple lines, devascularization, tissue trauma, and inadvertent presence of very tight staple lines [24]. Given these data, compared with endoscopic AEs, it is evident that APC treatment in a dilated gastrojejunal anastomosis is more reliable, with low rates of AEs.

Endoscopic follow-up was conducted every 4 weeks. According to the anastomosis healing process, a new APC procedure was generally performed 8 weeks after the first session. The current literature recommends intervals between 4 to 8 weeks, without defining the exact time to perform therapy, due to the scarce comparative data between the periods. The present study corroborates Baretta et al. [12], which demonstrated a 10 % deformity rate of gastrojejunal anastomosis with ulceration after 8 weeks of argon session. After 8 weeks, APC performance more accurately determines measurement of gastrojejunal anastomosis, facilitating performance of the procedure on healed mucosa and decreasing the rate of AEs.

We also evaluated possible histological and anatomical AEs, which may be a triggering factor for developing dysplastic or neoplastic cells due to repeated local cauterization. It could also be a limiting factor for early diagnosis of cancerous lesions due to superficial re-epithelialization and possible permanence of dysmorphic cells in deep tissue. In this case, no histological changes suggested neoplasia in patients undergoing APC. Dotti et al. [25] showed a correlation between potency and level of mucosal involvement (depth), analyzed by histology, after applying APC in esophageal mucosa affected by Barrett's esophagus. They observed that the higher the potency, the greater the deep mucosa; with 90 % of patients undergoing APC with 70 W, the deep mucosa was cauterized, different from patients with an APC 50 W rate of 60 %. These findings are consistent with Garrido et al. [26], which observed mucosa muscularis involvement when using higher amounts of energy after APC application over esophageal tissue.

We consider that the main limitation of this study was the absence of patient food intake records. Furthermore, the study did not monitor lifestyle, including physical activity. The literature has shown that all these factors must be considered during the weight loss process because they can be determinants of success of treatment [27, 28]. However, all volunteers were counseled about how to optimize these variables. These factors could provide additional answers to the findings presented here.

Conclusions

We concluded that APC effectively treats weight regain after RYGB in the short and medium terms. Additionally, it is a safe procedure with low AE rates. Nevertheless, a significant “new” weight gain was observed in the long term, highlighting the importance of long-term follow-up of patients after APC. Moreover, although the APC could be an additional tool against obesity, it is essential to consider that even the most invasive treatments may not result in long-term results. Therefore, a multidisciplinary team and family support are fundamental for the healthcare of these patients.

Competing interests

The authors declare that they have no conflict of interest.

Clinical trial

Brazilian Clinical Trials Registry (http://www.ensaiosclinicos.gov.br/). Longitudinal, Randomized and Blinded
U1111-1259-6021
TRIAL REGISTRATION: Longitudinal, Randomized and Blinded study The Universal Trial Number – UTN: U1111-1259-6021 at Brazilian Clinical Trials Registry (http://www.ensaiosclinicos.gov.br/)

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