Glucagon-Like Peptide-1 Receptor Agonists (Semaglutide) in conjunction with a diet and exercise program for the treatment of weight regain or weight loss plateau in Post-bariatric Surgery patients

Deeba Siddiqui, Indraprastha Apollo Hospital, New Delhi

Conflicts of Interest Dusclousure

I hereby declare that we have no potential conflict of interest to report

Glucagon-Like Peptide-1 Receptor Agonists (Semaglutide) in conjunction with a diet and exercise program for the treatment of weight recidivism or weight loss plateau in Post-bariatric Surgery patients

- About 20%–25% of patients experience weight regain (WR) or inadequate weight loss (IWL) following bariatric surgery (BS) and reduces treatment-associated health benefits.
- The efficacy of semaglutide for treatment of type 2 diabetes mellitus and obesity is well established, but their role in the treatment of weight regain after bariatric surgery remains to be defined

Weight regain (WR) defined as regain of weight that occurs after achievement of an initial successful weight loss (defined as EWL%>50%)

Insufficient weight loss (IWL) defined as<50% EWL

at 18 months after Bariatric Surgery

There is no standard definition for WR in the literature; however, most of the studies accept the definition of WR as 10 kg of weight gain after reaching nadir weight.

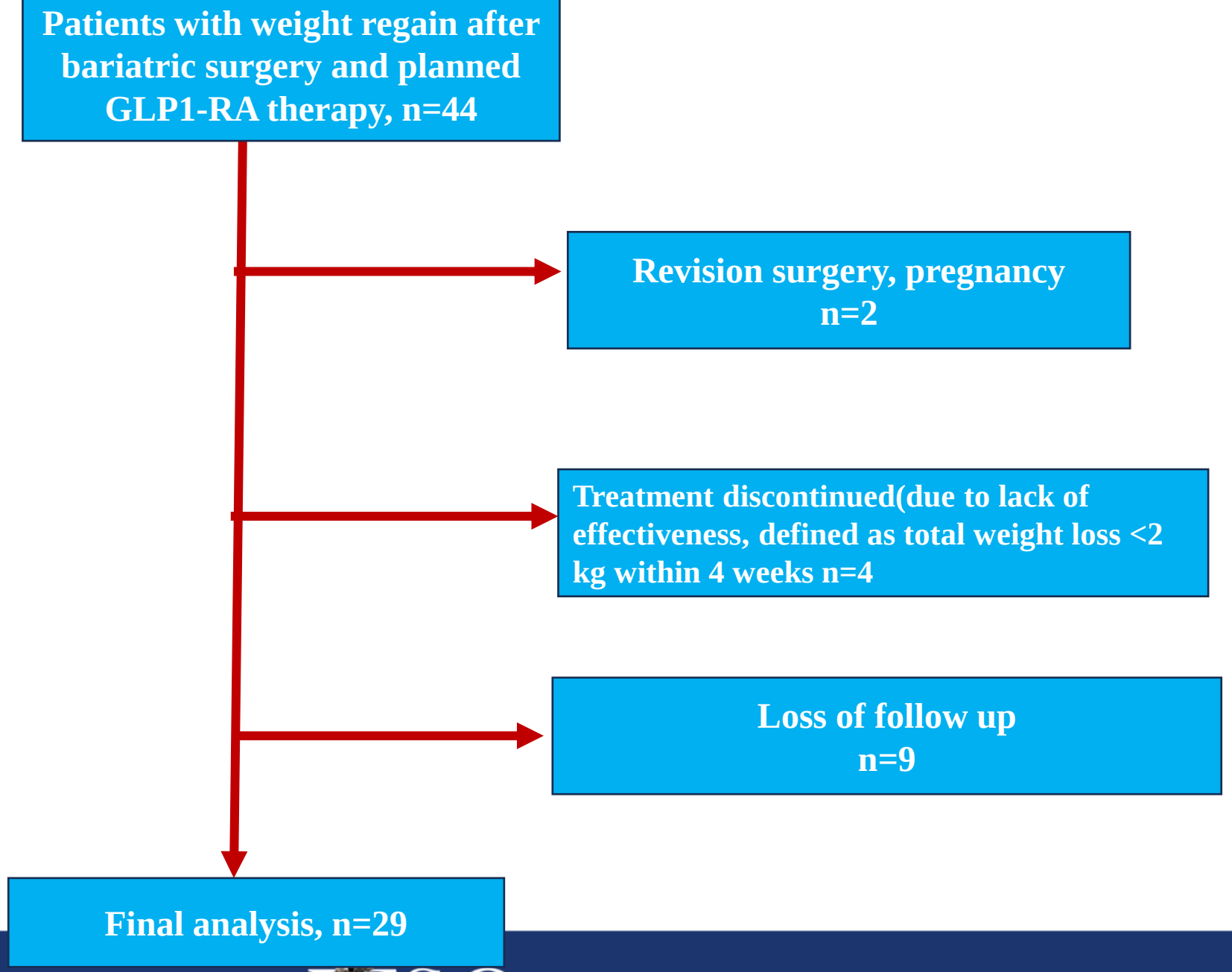
Aim:

- **The primary objective was to assess the change in total body weight and BMI and the percentage of weight loss after GLP1-RA intervention for 1 year.**

- **The secondary end point was safety, based on any therapy-related adverse events, including severity.**

Method:

- This was a single center **prospective observational study** conducted at Indraprastha Apollo hospital, New Delhi. Patients with weight regain or inadequate weight loss after bariatric surgery, until November 2021, were selected for this study
- A written informed general consent was present for all patients included in the study.
- Data on body weight and relevant clinical parameters were collected before and after 1 year of treatment with GLP1-RA.
- If clinically warranted, a potential anatomical cause for the weight regain (pouch-/stoma-dilation, gastro-gastric-fistula, or gastric sleeve dilation) was investigated with a barium meal test and/or an upper endoscopy.
- If an anatomical cause were identified, the choice between medical and surgical therapy would be thoroughly discussed with the patient.
- All patients undergoing bariatric surgery were regularly counselled by a bariatric nutritionist both pre- and post-operatively.
- Glucagon-Like Peptide-1 Receptor Agonists (Semaglutide) was administrated at a dosage of 3mg for the first 4 weeks. The dose escalation was performed according to clinical response and increased to 7mg after 2 weeks and finally administrated at a dosage of 14 mg


Patients with weight regain after bariatric surgery and planned GLP1-RA therapy, n=44
Revision surgery, pregnancy n=2
Treatment discontinued(due to lack of effectiveness, defined as total weight loss <2 kg within 4 weeks n=4
Loss of follow up n=9
Final analysis, n=29

Statistical methods

- Standard descriptive statistics were used for all study endpoints. Distributions of continuous variables were described with mean and standard deviation (SD).
- Categorical variables were described with absolute and relative frequencies.
- Normal distributed parameters were compared by type of surgery using Student's *t*-test.
- Categorical parameters were compared by using Chi-squared test.
- Continuous parameters between multiple visits were compared to baseline using fitting a mixed-effects model for repeated measures.
- Univariate logistic regression analysis was conducted to identify significant factors of successful weight loss defined as relative weight loss of ≥10% at 12 months follow-up compared to the baseline visit.
- Odds ratio with 95% confidence intervals and *p*-values were calculated.
- **The *p*-values below .05 were considered statistically significant.**

RESULTS

Patient characteristics at baseline

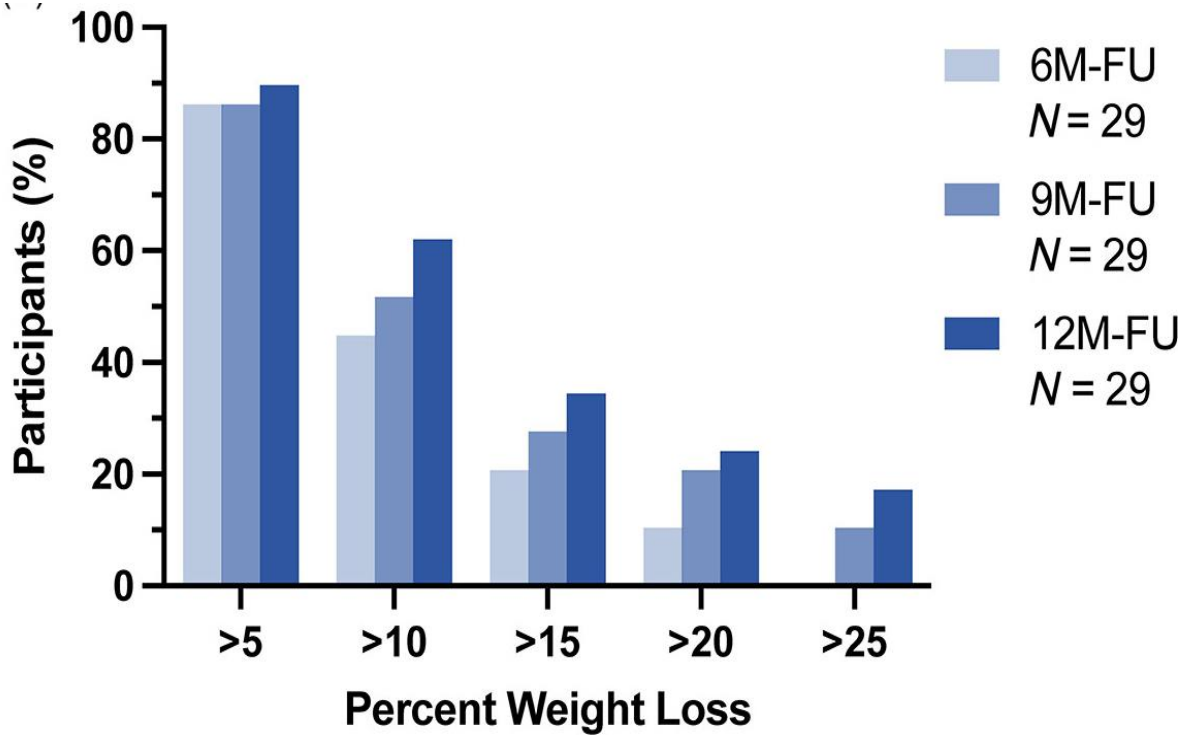
- Age was 48.5 ± 8.4 years (mean ± SD), 82.8% of patients were female. 62.1% of patients underwent SG, 37.9% underwent MGB as initial weight loss procedure.
- BMI prior to surgery was 50.4 ± 9.5 kg/m^2 (mean ± SD), **total weight loss after surgery was 23.4% ± 8.3%** (mean ± SD), maximum weight loss following BS was 30.7% ± 10.5% (mean ± SD).
- **Post-operative WR** after post-bariatric weight nadir and before adjunct semaglutide was **12.2% ± 15.4% (mean ± SD)**

TABLE 1. Anthropometric and biochemical characteristics at baseline by type of surgery.

	MGB (N = 11)	SG (N = 18)	Total (N = 29)	p-Value
Time from BS to initiation of semaglutide treatment (months)	81.6 ± 39.5	54.1 ± 56.7	64.5 ± 51.9	.024
Time from weight nadir to initiation of semaglutide treatment (months)	57.8 ± 32.9	23.8 ± 28.7	36.7 ± 34.2	.004
Total weight loss from BS to nadir (%)	−31.5 ± 10.7	−30.2 ± 10.7	−30.7 ± 10.5	.650
Weight regain from nadir to initiation of semaglutide treatment (%)	19.0 ± 16.5	8.0 ± 13.6	12.2 ± 15.4	.018

Weight loss outcomes at 12 months follow-up

Patients initiated semaglutide **64.5 ± 51.9 months (mean ± SD)** after BS at a BMI of **38.3 ± 6.1 kg/m²** (mean ± SD). After 12 months , total weight loss added up to **14.7% ± 8.9%** (mean ± SD, $p < .001$).

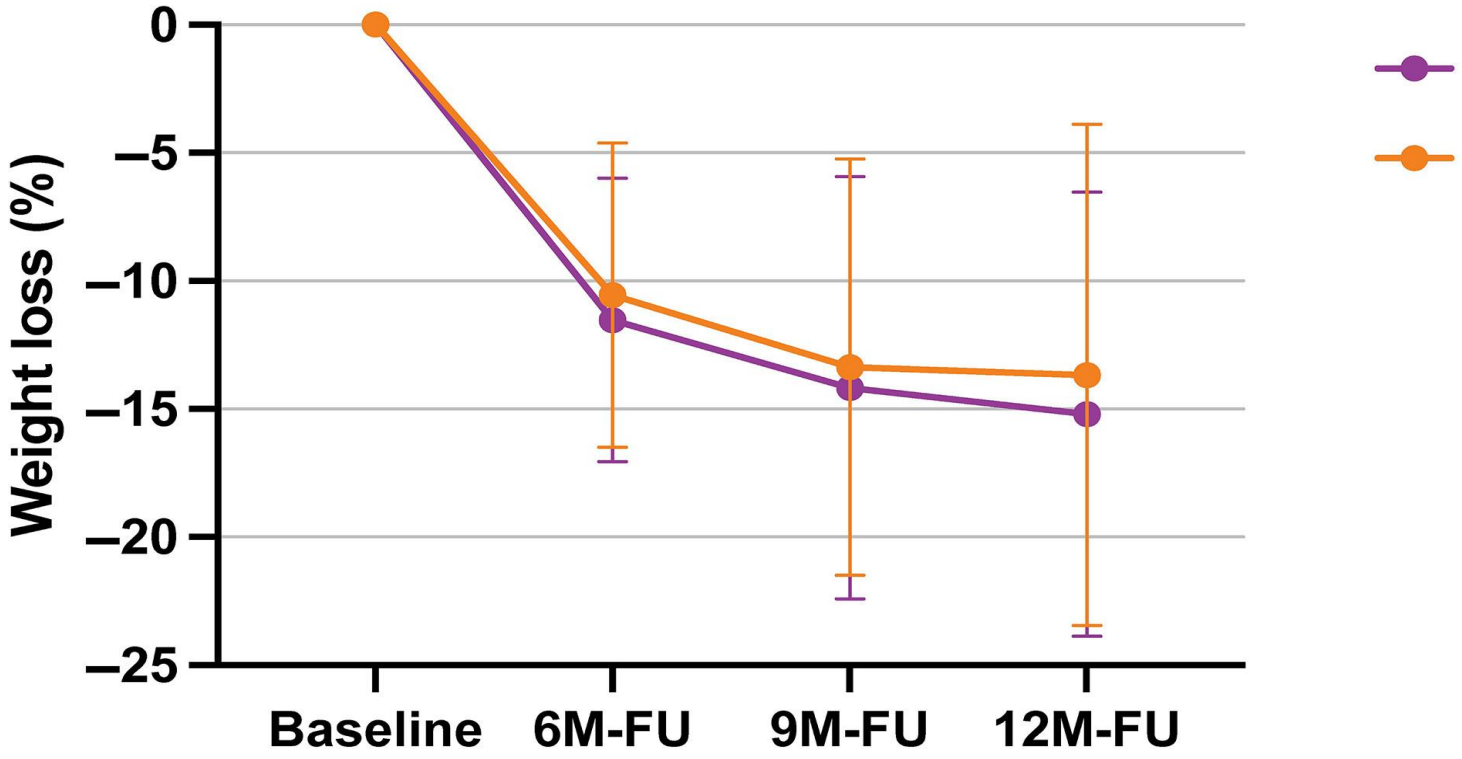


- **89.7% of patients reached >5% weight loss**
- **62.1% of patients reached >10% weight loss**
- **34.5% of patients reached >15% weight loss**
- **24.1% of patients reached >20% weight loss**
- **17.2% of patients reached >25% weight loss**

A) Weight loss (%) over time and (B) percentages of patients who reached weight loss of at least 5%, 10%, 15%, 20% and 25%, respectively, following adjunct treatment with oral semaglutide for 6, 9 and 12 months

Weight loss outcomes at 12 months follow-up depending on type of surgery

With regard to type of surgery, there were no significant differences in semaglutide-induced weight loss after 12 months between patients who had undergone SG versus MGB ($p = .96$). BMI and change in BMI prior to initiation of semaglutide was not significantly different between the subgroups.



Weight loss (%) over time following adjunct treatment with oral semaglutide by type of surgery. FU, follow-up; MGB, Mini gastric bypass; SG, sleeve gastrectomy. Results are expressed as means and standard deviation.

69% of patients ($n = 20$) were classified as having **WR**, **31% of patients** ($n = 9$) were classified as having **IWL.** Differentiating between these two groups**, no significant differences in weight loss response were found (15.0% ± 9.9% and 13.9% ± 7.0%; $p = .99$).**

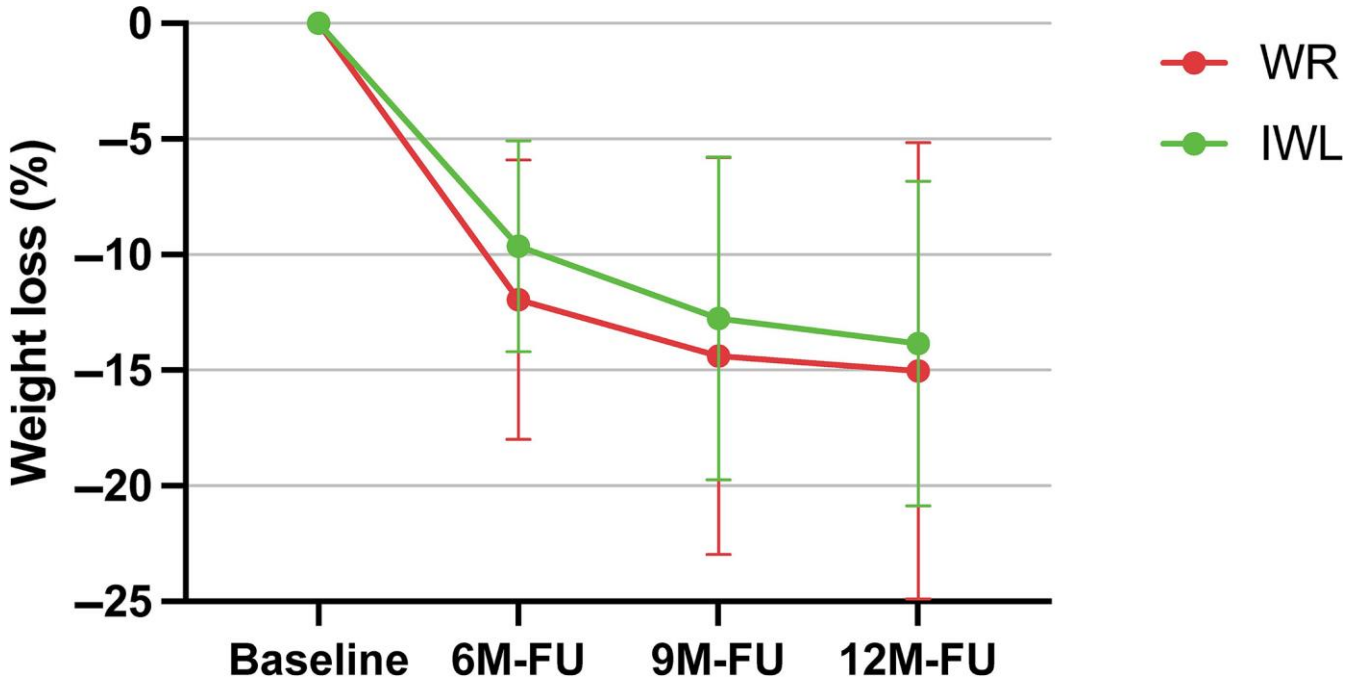


TABLE 2. Anthropometric and biochemical characteristics at baseline and follow-up visits.

	Baseline (N = 29)	6 M-FU (N = 29)	p-Value	9 M-FU (N = 29)	p-Value	12 M-FU (N = 29)	p-Value
Body weight (kg)	110.8 ± 22.2	99.2 ± 22.9	**<.001**	96.4 ± 25.4	**<.001**	95.4 ± 24.0	**<.001**
BMI (kg/m^2)	38.3 ± 6.1	34.5 ± 6.3	**<.001**	33.7 ± 7.4	**<.001**	33.0 ± 7.2	**<.001**
HbA1c (%)	5.4 ± 0.4	5.2 ± 0.2	**.048**	5.2 ± 0.3	.135	5.1 ± 0.4	**<.001**
Total weight loss (%)		−11.2 ± 5.6	**<.001**	−13.9 ± 8.0	**<.001**	**−14.7 ± 8.9**	**<.001**

Conclusions:

- After 12 months of treatment with semaglutide, total weight loss added up to 14.7% ± 8.9% (mean ± SD, $p < .001$). 89.7% of patients reached >5% weight loss, 62.1% of patients reached >10% weight loss, 34.5% of patients reached >15% weight loss, **24.1% of patients reached >20% weight loss and 17.2% of patients reached >25% weight loss**.

- GLP-1 receptor agonists (RA) were found to be more effective for treating post-bariatric weight regain than non-GLP-1-based pharmacotherapies regardless of surgery type.

- Differentiating between patients with WR and IWL, no significant differences in weight loss response were found in our cohort.


Thank you