

Dear Editor/Reviewer,

Thank you so much for your useful comments and suggestions on our manuscript entitled "Overview on the endoscopic treatment for obesity: A review" We have modified the manuscript accordingly using track changes, and detailed corrections are listed below point by point:

Reviewer #1:

Very well-written and narrative review in a topic of clinical importance.

Response: Thank you so much for your kind words! I'm glad to hear that you found the review valuable and well-written. It's always rewarding to know that the information is helpful in addressing clinical matters

Reviewer #2:

This issue is very interesting and has been extensively studied, with numerous reviews and meta-analyses focusing on outcomes related to weight loss and safety. Therefore, any new review should be a thoroughly review and should cover different topics people often don't do it

The Authors attempt to consolidate information from multiple reviews and metanalysis. However, there is a notable absence of critical discussions regarding indications comparing the different approaches, and suggesting which endoscopic procedures should be first indicated and when the others.

For instance, the actual role of intragastric balloons in obesity treatment should be commented.

The discussion of adverse events is short and superficial.

1.- The introduction of this review is overly lengthy and could benefit from being more concise, as it tends to repeat well-known data. The authors write "even if there are clinically significant comorbidities (metabolic, psychological, etc.), patients with a BMI of 35 kg/m² or over are not suitable for bariatric surgery . " Could you explain a little more the reasons why these patients are not suitable for bariatric surgery? Bariatric endoscopy

Response: Thanks for your valuable suggestion and reasons are added and it looks like, However, even if there are clinically significant comorbidities (metabolic, psychological, etc.), patients with a BMI of 35 kg/m² or over are not suitable for bariatric surgery. Only a small number of eligible patients can potentially benefit from bariatric surgery ^[15]. This may be due to various reasons. Firstly, the risk-benefit profile becomes less favorable as higher BMI levels often correlate with increased surgical complications, postoperative mortality, and reduced success rates ^[16]. Additionally, the potential benefits of surgery, such as weight loss and improvement in comorbidities, might be outweighed by the surgical risks and associated challenges in this specific BMI range. Moreover, alternative interventions, including lifestyle modifications, pharmacotherapy, and non-surgical interventions, might be considered more appropriate due to the complexities posed by the patient's heightened obesity levels. However, careful assessment of individual risks and benefits remains essential in determining the most suitable treatment approach. Lastly, advance studies have questioned the longevity of bariatric surgery due to the regular occurrence of weight regain and adverse effects ^[17].

2.- on page 6, the authors mentioned, "The drawbacks of IGBs, such as risks during insertion and removal, and unknown long-term weight loss benefits, prevent their widespread use [41]." Nevertheless, the text lacks commentary on the methods of balloon placement and withdrawal, as well as their association with complications. Specifically, there's no mention of whether conscious sedation or general anesthesia is used or should be used during balloon withdrawal (with or without anesthetic intubation) and their relationship with some complications.

Response: Necessary information is added and it looks like, Meanwhile, considering conscious sedation versus general anesthesia during balloon withdrawal, with or without anesthetic intubation, is pivotal due to its potential implications for procedural complications [42]. The choice between these approaches hinges on patient health status, procedure complexity, and anticipated discomfort. Utilizing conscious sedation may offer benefits like reduced risks associated with intubation but could lead to patient discomfort or inadequate sedation levels, potentially

increasing complications [43]. In contrast, employing general anesthesia with intubation might mitigate patient discomfort but could introduce intubation-related risks. Balancing these considerations is essential to optimize patient comfort and procedural safety during balloon withdrawal, and a comprehensive understanding of the relationship between sedation choices and associated complications is critical for informed decision-making. Meanwhile, utilizing a dual-channel gastroscope, specialized foreign body forceps, and a symmetrical snare designed for polyp removal enables a secure, efficient, and straightforward extraction of the balloon. This approach ensures the balloon is removed without any misplacement risk while maintaining patient comfort throughout the procedure [44].

3.- Regarding page 7, the phrase "Between 2016 and 2019, the number of IGB surgeries" requires clarification. What does "IGB surgeries" refer to? And "...Consensual management had an adverse event" what does it mean

Response: This phrase is modified for more clarification and it looks like, Between 2016 and 2019, according to the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) the number of IGB procedures reported decreased considerably (953 (0.62%) vs 418 (0.25%); $p < 0.0001$). Given the safety and efficacy of current bariatric surgery and novel pharmaceutical treatments for weight loss, the function of IGBs in treating obesity remains uncertain [52]

Meanwhile, Consensual management" typically refers to a management approach or decision-making process in which all relevant parties involved or affected by a particular decision or action are consulted, and their input is considered before reaching a consensus or agreement on the course of action to be taken. This approach aims to ensure that decisions are made with the collective agreement of those who have a stake in the outcome, thereby promoting cooperation, buy-in, and a sense of shared responsibility. It is commonly used to foster inclusivity and collaborative decision-making.

4.- Additionally, on page 8, when discussing a single balloon type (Orbera intra-gastric balloon), the authors stated, "the balloon implantation assembly is inserted directly into the stomach, and a volume of 500 to 700 mL saline solution." It's important adding to the text here that 5 ml of methylene blue should also be included , because the authors mentioned “..however, current practice mandates a very simple method of detection through observing any irregular change in urine output [58]. For the reader's clarity, it's important to indicate the reason why to choose the volume of inflation on 500 or 700 ml.

Response: Suggestion is incorporated and it look like,

Following a diagnostic endoscopy, the balloon implantation assembly is inserted directly into the stomach, and a volume of 500 to 700 mL saline solution (this volume range (500 to 700 mL) is chosen based on optimal balloon expansion and effective positioning within the stomach) with 5mL of methylene blue is used for balloon inflation via a closed infusion system, with the entire procedure being performed under direct endoscopic observation [57, 58].

5.- There's a lack of discussion on a significant issue: the role of intragastric balloons as a bridge before bariatric surgery, aimed at reducing BMI and potentially lowering the morbidity associated with bariatric surgery. Taking into a count the IGB is a well-known temporary weight loss device [36 this could be a perfect indication of IGB treatment The authors' reference to this issue is indeed quite limited, and only in the part of INTRAGASTRIC BALLOONS (AIR FILLED) with “They can also be used as a preoperative test before doing restricted bariatric surgery on patients. Furthermore, an intragastric device can be used as a "bridge treatment" before major surgery in individuals with severe obesity to lower the risk of operation-related complications [66].” However, there are many more data and considerations published in the literature with the fluid balloon to provide a more comprehensive analysis

Response: Additional discussion is added and it looks like,

Furthermore, IG balloons play a pivotal role as a transitional measure before bariatric surgery by serving as a bridge to reduce BMI and potentially mitigate the associated surgical risks. Intragastric balloons help patients achieve a lower BMI by facilitating

initial weight loss, which may lead to improved overall health and decreased comorbidities. This reduction in BMI can also contribute to decreased surgical complications during subsequent bariatric procedures. Acting as a preoperative intervention, intragastric balloons offer a safer trajectory for individuals with high BMI, allowing them to undergo bariatric surgery with potentially reduced morbidity and an enhanced surgical outcome.

6.- INTRAGASTRIC BALLOONS (AIR FILLED) there is needed of more technical information about: Gas Inflation: Provide specifics about the type of gas used for inflation of air-filled intragastric balloons. This could include mentioning whether it's regular air or a specific medical-grade gas mixture. Also, indicate the volume or amount of gas typically used for inflation and why. Mechanism of Inflation: Explain please the procedure or equipment utilized for inflating air-filled balloons. This could involve details about how the gas is introduced into the balloon, whether it's through a specific catheter.

Response: I really appreciate your suggestion and necessary information is added and it looks like,

Meanwhile, the balloon is inflated with a specific gas, such as air or a mixture of air and nitrogen, using a catheter or a small tube connected to the balloon. The gas inflates the balloon, causing it to expand and take up space within the stomach [41].

7.- COMPLICATIONS WITH IGBS Please include a comprehensive table detailing the types and rates of complications, as well as the causes of fatalities, would greatly enhance the clarity and completeness of the information. “ Esophagitis ,Upper Bleeding ,Untreatable Vomits by gastric or bowel obstruction , Perforation ,Dehydration Acute Renal Failure, Problems with Aerial Via Airway obstruction, choking” , and add any additional complications or causes of fatality that are relevant to your study. Remember to provide the specific rates.

Response: In table 1 adverse events were already mentioned, in most of the papers there were limited data related to complication rates that's why rates were not included.

8.- ENDOSCOPIC SLEEVE GASTROPLASTY (ESG) Page 15: "There were no intra-procedural complications, and around 2.3% of patients had serious post-procedure issues." Could you explain them? In the last paragraph of this page, the authors write, "Leaks, perforation, bleeding [115], better depth perception, better visualization [116], severe abdominal pain, and a perigastric collection [117] have been reported. Intraabdominal collection, refractory symptoms requiring ESG reversal, hemorrhage requiring transfusion or endoscopic intervention, pneumoperitoneum and pneumothorax, and pulmonary embolism [118], are among the serious adverse events..." If these are described complications of ESG, they should be commented and joined after the sentence "... and around 2.3% of patients had serious post-procedure issues"

Response: It is modified and look like,

Meanwhile, there were around 2.3% of patients had serious post-procedure issues; nevertheless, no deaths were documented [114]. Leaks, perforation, bleeding [115]. better depth perception, better visualization [115] severe abdominal pain and a perigastric collection [116] have been reported. Intraabdominal collection, refractory symptoms requiring ESG reversal, hemorrhage requiring transfusion or endoscopic intervention, pneumoperitoneum and pneumothorax and pulmonary embolism [117] are among the serious AEs that have been documented.

9.- Could you explain the TOGA acronym and also the differences with the POSE method and ESG? Please add some figures.

Response: TOGA acronym is explained while POSE and ESG were already explained. However, the difference in incorporated which looks like,

The POSE and ESG methods are distinct endoscopic approaches for obesity control. The POSE method involves the creation of tissue folds within the stomach to reduce its size and restrict food intake without removing tissue. In contrast, the ESG method involves suturing and narrowing the stomach's capacity, resembling a sleeve, to induce weight loss. While both methods are minimally invasive and avoid surgical incisions, the POSE method focuses on tissue folding, while the ESG method centers on suturing, leading to

different mechanisms of action. The choice between these techniques depends on individual patient characteristics, preferences, and specific weight loss goals.

10.- There is no comment about the lasting utility of the ESG procedure as time passes by, especially when comparing it with laparoscopic sleeve gastropasty.

Response: Suggestion is incorporated and it looks like,

In conclusion, as with any weight loss intervention, the success of the ESG procedure can be influenced by factors such as patient adherence to lifestyle changes, dietary habits, and individual metabolic factors. Comparing the lasting utility of ESG with LSG, a surgical procedure, the latter has a longer track record and more established data on long-term outcomes. LSG has demonstrated sustained weight loss and metabolic improvements over several years. However, it is essential to note that LSG is a more invasive procedure with potential surgical risks and complications. When evaluating the choice between ESG and LSG, patients and healthcare providers should consider the balance between the invasiveness of the procedure and the expected long-term outcomes, as well as individual patient preferences and medical considerations.

11.- It is necessary to comment and stress in detail any comparative study published in the literature , comparing ESG and Laparoscopic sleeve gastrectomy results ,AEs, and lasting outcomes , such as perhaps the only one commentary found in the text on page 15 “However, a study found laparoscopic sleeve gastrectomy to be more efficient then ESG as it improved weight related QoL significantly [114].

Response: Information is added and it looks like,

Furthermore, seven studies in a meta-analysis encompassed 6,775 patients, with 3,413 undergoing ESG and 3,362 undergoing LSG procedures. Notable disparities were observed in the percentage of %TBWL, all of which favored LSG over ESG. While there was a tendency toward a decreased occurrence of AEs with ESG compared to LSG, this distinction did not achieve statistical significance (risk ratio [RR] 0.51, 95% CI 0.23-1.11, $P = 0.09$). The frequency of new-onset gastroesophageal reflux disease (GERD) was markedly lower following ESG as opposed to LSG, at 1.3% compared to 17.9%, respectively (RR 0.10, 95% CI 0.02-0.53, $P = 0.006$) [117]. Moreover, a total of 2188 patients

(1429 for LSG and 759 for ESG) from sixteen studies were included in another meta-analysis. The mean percentage of %EWL was 80.32% (± 12.20 ; 95% CI; $p = 0.001$; $I^2 = 98.88$) for the LSG group and 62.20% (± 4.38 ; 95% CI; $p = 0.005$; $I^2 = 65.52$) for the ESG group. This represents an absolute difference of 18.12% (± 0.89 ; 95% CI, $p = 0.0001$) between the two groups. The variation in the average rate of AEs was 0.19% (± 0.37 ; 95% CI; $\chi^2 = 1.602$; $p = 0.2056$) [118]. Similarly, ESG results in weight loss comparable to LSG, with similar improvements in comorbidity resolution and safety profiles was shown in another study [119].

12.- Duodenal Jejunal bypass sleeve Could you explain what the technical procedure for DJBS is? Please add some images. “Serious AEs can be observed such as pancreatitis, GI bleeds, hepatic abscess, obstruction of the sleeve, and esophageal tears” could you add the rate of this AEs

Response: Technical procedure is incorporated and now it looks like,

The Duodenal-jejunal bypass sleeve, known as DJBS is introduced using endoscopic and fluoroscopic methods. This implant consists of a non-porous fluoropolymer sleeve, temporarily anchored within the duodenal bulb and extending approximately 80 cm into the small intestine, typically ending in the proximal jejunum [135, 136]. It allows chyme to move from the stomach to the jejunum without contacting the duodenum. By not allowing mixing with pancreatic exocrine secretions and bile in the jejunum, it replicates a duodenal-jejunal bypass and promotes weight reduction through malabsorption [137]. Which has similarities to Roux-en-Y gastric bypass (RYGB) and this combined mechanism aims to achieve weight loss by reducing calorie intake and altering nutrient absorption patterns. The DJBS procedure offers a potentially reversible option for individuals with obesity seeking to manage their weight and improve metabolic health [138].

We thank the reviewer for conducting an in-depth analysis of our study and providing helpful suggestions. Adding the pictures would undoubtedly be of interest. However, we have decided to maintain a text-based approach for this particular work. The content best conveys ideas and information through written explanations and descriptions.

Nonetheless, we do recognize the importance of visual aids in specific contexts, and we will certainly keep this in mind for future projects. Your input has encouraged us to continually explore ways to enhance our communication methods and make our content as accessible as possible to a broader audience.

Available AE rates are included and it looks like,

In total there 3.7% AEs Serious AEs can be observed such as pancreatitis (2 cases), GI bleeds (7 cases), hepatic abscess, obstruction of the sleeve, and esophageal tears [144]. There were no reported fatalities. Mild AEs primarily comprised nausea, vomiting, and anchor ulceration. Meanwhile, the attachment point of the DJBL was responsible for inducing or potentially inducing 85% of the SAEs [145].

13.- There are not any comment and discussion about duodenal mucosal resurfacing

Response: The study focuses on more established endoscopic treatments for obesity. DMR might not have been a prominent or widely adopted intervention within the scope of the review's timeframe as it is mainly used and recommended for Type 2 diabetes. That's why that particular technique was not discussed in detail.