AGA Clinical Practice Guidelines on Intragastric Balloons in Management of Obesity

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Abbreviations used in this paper: AGA, American Gastroenterological Association; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MD, mean difference; OR, odds ratio; RCT, randomized controlled trial; RR, relative risk; SOC, standard of care; TBWL, total body weight loss; EWL, excess weight loss

Obesity is a global pandemic, affecting about 40% of adults in the United States. There is a vast area of an unmet need, as only 1.1% of eligible obese patients are receiving primary bariatric surgery. Endoscopic bariatric therapies have evolved as an attractive tool for weight loss, however, less than 5% of obese patients seeking a weight loss therapy are aware of endoscopic weight loss options. Intragastric balloons (IGB) launched nearly four decades ago have recently gained more popularity with multiple new devices introduced into the U.S. market. While IGBs are a plausible option for patients seeking weight loss, it is essential for providers, patients and healthcare teams to understand how IGBs compare to lifestyle modifications with respect to important patient outcome measures such as weight loss, improving metabolic parameters, and lessening comorbid medical conditions. This guideline can assist both patients and providers in determining if IGBs is a weight loss option that should be considered and/or pursued.

Methods

This guideline on the intragastric balloon was developed by the AGA Institute's Clinical Guidelines Committee and approved by the AGA Governing Board. It is accompanied by a technical review that provides a detailed synthesis of the evidence from which these recommendations were formulated. To get a better understanding of these guidelines, we recommend reading the accompanying technical review. Development of this guideline and the accompanying technical review was fully funded by the AGA Institute without additional outside funding.

Guideline panel composition, Funding, Conflict of Interest

Members of the Guideline Panel and Technical Review Panel were selected by the AGA Governing Board in consultation with the Clinical Guidelines Committee with careful consideration of all Institute of Medicine recommendations for clinical guideline development. A patient representative was also included in the development and review process and had no recommended changes. The guideline and accompanying technical review underwent independent peer review, and a 30-day open public comment period; all comments were collated by the AGA staff and were reviewed and carefully considered by the Guideline Panel and Technical Review teams, respectively. Changes were incorporated in revised documents, and where changes were not accepted, a thoughtful response document was created. In accordance with the Clinical Guidelines Committee policies, all clinical guidelines are reviewed annually at the AGA Clinical Guideline Committee meeting for new information. The next update for these guidelines is anticipated in 3 years from publication (2024).

This guideline was developed utilizing a process outlined previously. The AGA process for developing clinical practice guidelines follows the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach and best practices as outlined by the National Academy of Medicine (formerly Institute of Medicine).[1]

Formulation of Clinical Questions

A priori, the Guideline Panel (Gastroenterologists, T.M, L.D, E.H, Nutritionist L.T) and a methodologist (M.H.M), GRADE experts (S.S,) identified and formulated clinically relevant questions about the use of intragastric balloons in obesity. Each research question identified the population, intervention, comparison, and patient-important outcomes. The Technical Review Panel initially reviewed and assessed relevant systematic reviews that addressed the clinical questions, updating high-quality systematic reviews through January 2020 to inform the recommendations when possible. (CITE TR)

For situations in which there was either no recent systematic review available or the recent systematic review was not deemed high quality, the Technical Review Panel conducted the systematic review de novo. The findings from each systematic review were assessed using the GRADE approach and presented in an evidence profile. GRADE approach breaks down the clinically relevant questions in to a series of statements phrased in the PICO format that defines the population (P) under study, the intervention (I) under consideration, the comparator (C) against which the intervention is assessed and the outcome (O) worthy of evaluation.[1] It is important to state that if comparator is not stated, then it is implied that the management strategy is compared against 'potentially equivalent strategy' or 'do nothing'

Development of Recommendations

The Guideline Panel and the authors of the technical review met face to face on March 8, 2020 to discuss the findings from the technical review. After this meeting, the Guideline Panel (T.M., L.D, L.T, E.H) independently formulated the guideline recommendations; the Technical Review Panel was not involved in the formulating or finalizing the recommendations. The certainty of available evidence and the strength of recommendation are provided with each PICO statement. The certainty of the evidence supporting the PICO statement is described on a 4-point scale from high to very low. (**Table 1**). A very low rating indicates great uncertainty regarding the estimate of effect.

Evidence Review

While the certainty of evidence was a key factor in determining the strength of the recommendations (**Table 2**), the Panel also considered the balance between the benefits and harms of the interventions, as well as patient's values and preferences, resource use (i.e., cost), heath equity, acceptability, and feasibility (the Evidence to Decision Framework). A 'strong' recommendation supports a clinical decision that should apply to most patients most of the time, whereas a 'conditional' (also called "weak" in some settings) recommendation implies that the decision is more nuanced and that some patients could be managed with a different approach. The recommendations, certainty of evidence, and strength of recommendations are summarized in Table 3.

External Review

The guideline and technical review went through a 3-day public comment period between xx 2020 to xx 2020. AGA staff collated the comments, the Guideline Panel deliberated in their response and when appropriate modified the document text. We hope to provide clinicians with clear guidance regarding the intragastric balloon use in management of obesity. The target audience of this guideline includes health care providers and patients. In addition, we were not able to assess the non-endoscopic balloons, as this is still not available in United States.

Recommendations

A summary of all of the recommendations in this guideline is provided in **Table 3**.

IGB therapy as a weight loss intervention

1. In obese individuals seeking a weight loss intervention, AGA suggests the use of IGB therapy with life style modification over life style modification alone.

(conditional recommendation, moderate certainty).

Implementation remark: **Fluid filled balloons may be associated with higher efficacy and lower tolerability than air fluid balloons. A shared decision making is suggested for determining device choice.**

Rationale: First, across four important outcome measures related to weight loss, IGBs perform better than lifestyle modifications or standard of care (SOC) for individuals seeking to lose weight. With respect to weight loss, randomized controlled trials (RCT) have demonstrated that IGBs led to more sustained weight loss at three-, nine- and twelve-months compared to patients treated with SOC alone; however, the amount of weight loss incrementally decreased for each

successive time period. For example, pooled data from seven RCTs showed IGBs resulted in patients losing 15.46 lbs. (95% CI 10.42-20.51) at three-months, three RCTs illustrated that IGBs led to 13.12 lbs. of weight loss (95% CI 10.53-15.70) at nine-months and two RCTs reported weight loss of 9.76 lbs. (95% CI 6.38-13.14) for patients using IGBs at twelve-months versus SOC. Similarly, percent total body weight loss (TBWL) improved at three-, nine- and twelve-months for patients who received IGB therapy compared to those undergoing SOC with the greatest percentage total body weight loss observed at three months (6.89%, 95% CI 4.09-9.70). IGBs were more effective than SOC at all three time periods when examining percent excess weight loss (EWL) with again the three-month time frame showing the greatest benefit (18.55, 95% CI 13.94-23.16). Finally, obese patients who received IGB therapy had a significantly greater response of both 5 and 10% TBWL as opposed to those who underwent only SOC interventions for weight loss. Three RCTs showed 85.1% of individuals who received IGB therapy achieved 5% TBWL (versus 34.6% for SOC) whereas four RCTs demonstrated that 61.9% of patients with an IGB realized 10% TBWL compared to just 13.9% for SOC therapy over a 6-8-month time period. Thus, patients who utilize an IGB for weight loss therapy attain greater weight loss than SOC/lifestyle modification therapy over a one-year time frame.

Second, several metabolic parameters and medical comorbidities are improved in the short-term in patients who utilize IGBs compared to non-invasive measures for weight loss. Pooled data from five RCTs and eighteen observational studies illustrated that IGB therapy significantly lowers both HgbA1c and fasting blood glucose (FBG) levels more so that non-invasive therapy alone. In particular, greater benefit was observed in patients with a FBG level over 100 mg/dl, HgA1c greater than 6.5% and in patients with a body mass index above 40 kg/m^2. Mixed results were shown with respect to improving patient's lipid profiles; while no benefit was realized in reducing triglycerides for those patients that used IGB therapy, there was a decreasing trend of low-density lipoproteins in obese patients using IGBs. Improving liver function test abnormalities are also observed in patients who use IGBs for weight loss with ALT values decreasing by 9 U/I and AST values lowering by 3 U/I. Finally, diabetes, hypertension and dyslipidemia all achieved remission to a statistically significant greater degree in patients who utilized an IGB for weight loss as opposed to those patients who pursued a non-invasive approach. Taken together, current data suggests that IGB therapy improves laboratory abnormalities and medical diseases associated with obesity to a better degree than SOC alone.

Third, early IGBs were associated with a number of devastating adverse events [2,3] that resulted in their removal from the U.S. market in the 1980 and 1990s. Hence it is crucial to better understand adverse events associated with newer versions of IGBs in the last two decades. Early removal of IGBs was noted in 9.4% of patients with the most common reasons being device intolerance (e.g., sense of fullness) and symptomatic intolerance (e.g., epigastric pain, reflux, nausea, emesis). Seven RCTs were examined to assess the outcomes of serious adverse events associated with intragastric balloon therapy. More serious adverse outcomes were observed in patients who received IGB therapy (5.6%) compared to those in the SOC groups (1.1%) (RR 3.07, 95% CI 1.16-8.11). Yet, serious adverse events were relatively rare in patients receiving IGB treatment and mostly included injury to the gastrointestinal tract such as perforation (0.3%), esophageal mucosal injury (0.8%), gastric ulcer/bleeding (0.76%) and gastric outlet/bowel obstruction (0.12%). Over a 6-8-month period in patients with an IGB in place, no deaths were

reported in seven RCTs. Post-marketing surveillance of IGB has reported additional adverse events of hyperinflation, acute pancreatitis and death.

Lastly, various models of IGBs are available and can vary by filling medium (gas or liquid). A meta-analysis of 22 RCTs showed that fluid filled IGBs were associated with nearly 3% more weight loss compared to gas filled balloons. In particular, all three current models of the fluid filled balloons were demonstrated to be better than sham whereas only one of the two gas filled balloon models were better than sham. Overall, fluid filled IGB were more likely to be superior than air-filled IGBs. The systematic review referenced above has shown numerically higher rate of adverse events with fluid-filled balloons than gas-filled balloons; suggesting better tolerability of gas-filled balloons. Consequently, providers and patients together should assess the best available evidence, balance risk and harms and include patient preferences when determining whether to use a fluid or air filled IGB. Overall, the panel rated the quality of evidence as moderate.

2. In obese individuals undergoing IGB therapy, AGA recommends moderate to high intensity concomitant life style modification interventions to maintain and augment weight loss (strong recommendation, moderate certainty).

Rationale: Few studies have examined lifestyle modifications to maintain and/or enhance weight loss in obese patients who have had an IGB placed. Of the available literature, diets were the primary lifestyle modification that was examined with respect to improving weight loss once an IGB was placed and to maintain weight loss once the balloon was removed. One RCT randomized 80 obese patients to a low-calorie diet versus a very low-calorie ketogenic diet after having had an IGB in place for 2 months. After 6 months, the very low-calorie ketogenic diet resulted in greater mean weight loss and %EWL than the low-calorie diet (MD 7.1, 95% CI 6.30-7.90 and 12%, 95% CI 10.66-13.34, respectively). In addition, patients who underwent IGB placement for weight loss and continued with a moderate to high intensity diet 6 months after therapy were noted to have ongoing weight loss (17 kg) and BMI reduction (6 kg/m^2). While diet does augment and sustain weight loss in patients receiving IGB therapy, it's unclear if other lifestyle modifications (e.g., exercise) would have the same impact and is an area that deserves further investigation. Overall, the quality of evidence for this recommendation was moderate.

3. In individuals undergoing IGB therapy, AGA recommends concomitant treatment with proton pump inhibitors (strong recommendation, moderate certainty)

Rationale: Given the mucosa of the GI tract can be eroded and potentially bleed during and after the placement of IGBs, questions have arisen around the prophylactic administration of proton pump inhibitors (PPI) in individuals undergoing IGB therapy. Unfortunately, no RCTs have directly assessed patient outcomes with respect to PPI use in patients with IGB placement. However, indirect evidence suggests that: 1) PPIs reduce the risk of re-bleeding in patients with high-risk bleeding stigmata in the upper GI tract[4,5] and 2) in RCTs where patients received an IGB and were administered PPI therapy, there were lower device/non-procedure related serious adverse events, especially as it pertained to upper GI bleeding. PPIs are postulated to have risks of their own both in the short and long term[6-8]; it is therefore imperative that the lowest dose, frequency and duration of PPIs be used in patients undergoing IGB therapy. Overall, the quality

of evidence was moderate for concomitant PPI treatment. Future studies that include a comparator group and assess the optimal dosing, frequency and duration of PPI administration in obese patients receiving IGB therapy are warranted.

4. In individuals undergoing IGB therapy, AGA suggests using the intraoperative anesthetic regimens associated with the lowest incidence of nausea along with perioperative antiemetics. AGA suggests a scheduled antiemetic regimen for 2 weeks after IGB placement (conditional recommendation, low certainty).

Implementation remark: Evidence is insufficient to recommend a specific antiemetic regimen. The choice of regimen is based on institutional policy, clinical context and availability.

Rationale: In individuals undergoing IGB therapy, the panel suggests using the intraoperative anesthetic regimens associated with the lowest incidence of nausea along with perioperative antiemetics. Following IGB placement, the panel suggests a scheduled antiemetic regimen for 2 weeks. The specific antiemetic regimen should be based on institutional policy, clinical context, and availability. Two randomized controlled trials assessing antiemetic efficacy following IGB placement were identified. The first study compared a therapeutic regimen of midazolam and ondansetron versus ondansetron alone for preventive treatment of nausea/vomiting and found that combination therapy of midazolam and ondansetron trended towards outperforming ondansetron alone (RR 0.57; 95% CI 0.32,1.02).[9] Further, early balloon removal rate was lower in the midazolam and ondansetron arm compared to the ondansetron alone arm (0/29 and 3/28, respectively; RR 0.14, 95% CI 0.01, 2.56). The second study compared mean vomiting incidence between Alizapride, Tropisetron, and Tropisetron with droperidol, but due to limited availability of these agents in the United States it was not applied to this recommendation.[10] Due to limited direct evidence, RCTs assessing efficacy of anti-emetics in any restrictive bariatric surgery were considered.

Overall, the quality of evidence for this recommendation was low for antiemetic treatment of nausea in IGB. The two studies specific to this recommendation in IGB were found to have a serious risk of bias, indirectness, and imprecision. Additionally, when the search was expanded to include antiemetic therapy across bariatric surgery interventions, the quality of evidence was found to be low to very-low quality.

5. In individuals undergoing IGB therapy, AGA suggests against perioperative laboratory screening for nutritional deficiencies (conditional recommendation, low certainty).

Rationale: The panel suggests against perioperative screening for nutritional deficiencies in individuals undergoing IGB therapy. No direct evidence was identified on perioperative laboratory screening for nutritional deficiencies in individuals undergoing IGB placement for weight loss. Additionally, no indirect evidence from other restrictive bariatric procedures was identified regarding perioperative laboratory screening for nutritional deficiencies.

A number of peri-operative deficiencies have been identified in observational sleeve gastrectomy or gastric bypass surgery studies to date: thiamine, folate and magnesium deficiencies have been reported. Five studies identified report a prevalence of thiamine deficiency in peri-operative IGB

ranging from 0-29%. Four studies identified report a prevalence of peri-operative folate deficiency ranging from 0-24%.(CITE TR) In three pre-LSG procedure cohorts, no patients were found to have hypomagnesemia.(CITE TR)[11-13]

Overall the quality of evidence for this recommendation was low for perioperative laboratory screening for nutritional deficiencies. Observational studies suggest a potential for peri-operative nutritional deficiencies, however, and clinical judgement should be used on an individual basis regarding perioperative screening for nutritional deficiencies.

6. AGA suggests 1-2 multivitamins after IGB placement (conditional recommendation, very low certainty).

Rationale: The panel suggests 1-2 multivitamins after IGB placement. No direct evidence was identified for prophylactic dosing of multivitamin supplements post-IGB. Therefore, the panel evaluated the role of prophylactic dosing of multivitamins after IGB placement or similar restrictive gastric bypass procedures on a number of specific nutrient deficiencies: thiamine, folate, magnesium and potassium. Among 3 studies reporting a pre-operative thiamine deficiency prevalence of 0-29%, prophylactic dosing of 1-3 multivitamin tablets/day resulted in post-operative thiamine deficiency prevalence of 0-9%.[11,14,15] CITE TR Additionally, a single study reported maintenance of a normal pre-operative thiamine level at three months post-operatively with a daily multivitamin regimen.[16] Two studies in restrictive bariatric surgery cohorts, demonstrate maintenance of a normal pre-operative folate level for 3-12 months after surgery with 1 multivitamin per day prophylaxis.[13,17] Furthermore, there appears to be a potential for de-novo development of a folate deficiency if no prophylaxis is given in a subset of patients (6-9.2%).[18,19]. In three post-LSG procedure cohorts, in whom 1-2 multivitamins with minerals were recommended, no patients (N=205) were found to have hypomagnesemia up to 5 years after the procedure.[11-13]CITE TR Two single arm cohort studies provide evidence for the potential development of asymptomatic hypokalemia from vomiting 1-week post-IGB placement (6.8-8.5%).[20,21] Whether or not these patients were on a multivitamin was not reported. CITE TR

Overall the quality of evidence for was very low for prophylactic use of 1-2 multivitamins after IGB placement. Observational studies suggest a potential for post-operative nutritional deficiencies that may be preventable with multivitamin therapy.

7. After IGB removal, AGA suggests subsequent weight loss or maintenance interventions that include dietary interventions, pharmacotherapy, repeat IGB or bariatric surgery. The choice of weight loss or maintenance method after IGB is determined based on patient's context and comorbidities following a shared decision-making approach (conditional recommendation, low certainty).

Rationale: Having an open discussion with patients about the risks, benefits and alternatives of each weight loss management strategy is required for clinical practice. In patients who have had their IGB removed, the panel suggests subsequent weight loss or maintenance therapies that include dietary interventions, pharmacotherapy, sequential IGB, or bariatric surgery. The choice of therapy is based on open discussions with patients about their clinical status, their value and preferences, and safety profile of various strategies in a shared decision-making approach.

Two randomized controlled clinical trials provided evidence with respect to pharmacotherapy in addition to IGB. One RCT studied sibutramine 10 mg/day versus moderate/high intensity diet as maintenance therapy for 6 months after IGB removal. At the end of the study at 1 year, both groups reported significant, progressive weight loss of 17 kg and more than 6 kg/m^2 decrease in BMI. Pharmacotherapy fared slightly better than moderate/high intensity diet (TWL >10%: RR 1.50, 95% CI: 0.81, 2.78; WL in kg: MD 0.20 kg lost 95% CI: 2.01 gain, 2.41 lost; Decrease in BMI: MD 0.30 kg/m2 decrease, 95% CI: 0.55 increase, 1.15 decrease). [22] A second randomized controlled clinical trial studied liraglutide 3 mg/day in addition to IGB versus IGB alone for 6 months. This study showed that the pharmacotherapy arm performed better than IGB alone (TWL 10%: MD 14.72%, 95% CI: 8.81, 21.26; WL in kg: MD 3.8 kg lost, 95% CI: 2.43 lost, 5.17 lost; Decrease in BMI: MD 1.32 kg/m2 decrease, 95% CI: 0.92 increase, 1.72 decrease) (Evidence Profile: Medication). CITE TR

Evidence regarding sequential IGB therapy was based on two randomized controlled clinical trials CITE TRwhich evaluated sequential IGB versus IGB for 6 months followed by low calorie diet for 7 months. When the study ended at 13 months, patients who underwent a second IGB experienced a greater BMI reduction compared to individuals without a second IGB (BMI MD 5.49 kg/m^2 decrease, 95% CI: 4.82, 6.16). Non-RCT studies also demonstrated a trend towards greater BMI reduction favoring sequential IGB. However, risks and complications tend to be more frequent in patients with a second IGB or prolonged IGB use.

One observation comparative cohort study served as the primary source of evidence regarding bariatric surgery as a weight loss maintenance method after IGB therapy. Comparing patients who underwent bariatric surgery (Lap-band, LAGB, or duodenal switch) after IGB with patients who refused any weight loss maintenance strategy, the bariatric surgery group reported a delta of 16.6. kg/m^2 reduction in BMI and a delta of 42.5% EWL at 12 months. [23] One RCT and three observational studies offered evidence for effectiveness and safety of IGB prior to laparoscopic gastric band placement (LGBP). A small benefit was seen using IGB prior to surgery in reducing length of hospitalization stay by one day, lowering the risk of intraoperative risks and moderate to severe post-operative complications.

Overall, the panel rated the quality of evidence as low. While RCTs involving dietary intervention, pharmacotherapy, and sequential IGB were well conducted, the quality of evidence was rated lower due to the imprecision as a result of a small number of subjects and a short follow-up period. Furthermore, the efficacy and safety of sequential IGB and bariatric surgery strategies were informed by observational studies.

Implementation Considerations:

Intragastric balloon therapy can be an effective tool in the management of obesity and we hope to provide clinicians and patients with clear guidance regarding its use. Successful implementation of IGB during the active weight loss phase and maintenance phase often occurs with concomitant therapy, such as life style modifications, pharmacological agents, sequential IGB or bariatric surgery. These strategies implemented in conjunction with IGB lowers the risk of weight gain recidivism.

With the exception of the panel's acknowledgement that fluid filled balloons may be associated with higher efficacy and lower tolerability than air fluid balloons (recommendation #1), the panel

makes no recommendations on specific IGB devices. This determination is best made in a shared decision-making approach while considering the patient's values and preferences, balancing benefits and harms within the patient's clinical and behavioral context, cost, and availability. Likewise, these factors are also critical in guiding the appropriate selection for concomitant lifestyle modifications, pharmacotherapy, or sequential procedures.

Discussion:

The role of gastroenterologists in the management and treatment of weight loss in obese patients has evolved over the last four decades. Part of this changing role is driven by the advancement of intragastric balloons which are devices placed endoscopically in the outpatient setting and serve as a restrictive form of weight loss therapy for patients. Therefore, it is imperative that gastroenterologists understand the growing body of literature surrounding these devices; in particular, it's essential to understand not only the role that providers play in choices for weight loss therapy but also the effectiveness, safety, and patient and provider experiences with these devices. A better understanding of this information will allow gastroenterologists to create a more patient-centered approach whereby providers and patients collaboratively reach evidence-based and value-congruent decisions on the use of IGBs.

Significant improvements have been observed in obese patients using IGB with respect to a number of critical weight loss outcomes. Intragastric balloons lead to greater weight loss, improve metabolic laboratory abnormalities and changes the trajectory of several medical comorbidities associated with weight loss; clearly IGB therapy (with lifestyle medication) is superior to lifestyle modifications at initial and maintenance of weight loss for patients in the short-term (within at least 12 months of placement). While many questions surrounding IGBs have been answered, studies involving IGBs reveal many shortcomings; many conclusions were drawn as a result of indirect evidence, a number of studies lack a comparator group, small sample sizes were included, selection bias was present in several studies and there was a low reporting of several outcomes across many of the studies. Future work in this area needs to focus on larger RCTs that examine the short and long term efficacy of IGBs with respect to obesity related comorbidities (e.g., hypertension, diabetes, non-alcoholic steatohepatitis, cardiovascular disease), the long-term impact of single IGB implantation, predictive modeling for patients who may be non-responders or at higher risk of having adverse event(s), comparing IGBs efficacy with other short-term weight loss devices/procedures, and finally, cost-effectiveness studies of IGBs are necessary to more fully understand the entirety of the impact of these devices. One final question that remains open is where IGB therapy falls in the algorithm for obese patients seeking to lose weight. More information is required to better understand if IGB alone, sequentially and/or with concomitant therapies may be sufficient for some patients while in other patients it may serve a more adjunctive role such as a bridge to longer-term weight loss interventions such as bariatric surgery. While the short-term benefits of IGBs show them to be effective and safe in obese patients seeking to lose weight, the data remains unclear if such benefits are sustained in the longer term.

Intragastric balloons have been on the U.S. market since 1982, yet very few guidelines or consensus documents have specifically addressed the efficacy, safety and role that IGBs play in weight loss therapy. This guideline incorporates the most recent literature and evidence on IGBs and using GRADE methodology provides several evidence-based recommendations as it pertains

to IGBs. One question that arises is how this guideline fits in with other published work. In the U.S., two guidelines have been generated: a position statement by the American Society for Metabolic and Bariatric Surgery (ASMBS)/Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) (2016)[12], and the American Society for Gastrointestinal Endoscopy (ASGE)[24] systematic and meta-analysis assessing PIVI thresholds for adopting endoscopic bariatric therapies (2015). The ASGE position statement focused only on one IGB (i.e., ORBERA) and discovered that it resulted in a decrease of the percentage of excess weight loss and percentage of total body weight loss over a twelve-month period, serious adverse events being infrequent and a 7% early removal rate. On the other hand, the ASMBS/SAGES consensus statement examined two IGBs (i.e., ORBERA and ReShape). Here, they also illustrated that adverse events were rare (e.g., bowel obstructions, perforation and death), voluntary removal rate of 4.2-7.0%, and demonstrated efficacy at reducing percentage excess weight loss, total body weight loss and improved liver histology in patients with non-alcoholic steatohepatitis. On the international stage, a Brazilian consensus statement [25] based on experiences of 40,000 IGB placements, provided guidance on indications (i.e., age and BMI), contraindications for placement, pre- and post-procedure evaluation with a multi-disciplinary team, medications to utilize to relieve symptoms (i.e., anti-emetics, steroids, analgesics and proton pump inhibitors) and a review of adverse events. The strength of our guideline is that it rigorously examined the data and applied a validated tool to synthesize the data, included all current IGBs on the market and assessed efficacy in a number of areas (laboratory values, metabolic parameters and medical diseases), safety (both major and minor adverse events) and tolerability. This comprehensive document validates and expands upon the conclusions of previous position statements and provides greater clarity on IGBs with respect to additional areas of concern to patients, providers and healthcare teams.

Future Research Needs and Evidence Gaps:

These recommendations highlight the need for additional research on the use of intragastric balloons for management of obesity. Our TR suggests that IGB therapy with lifestyle modification is an effective weight loss intervention. Further, IGB therapy seems to result in improvements in metabolic parameters and medical comorbidities. Evidence gaps include long-term efficacy of IGB therapy compared to SOC beyond one year. Given the incremental trend towards a decrease in weight loss observed in the period 3-12 months after placement, there is a need to determine efficacy of IGB therapy beyond one year, both with regard to weight loss but also metabolic parameters and medical comorbidities. Consideration should be given to variables such as the filling medium (fluid vs. air) and the potential efficacy of ongoing dietary intervention, pharmacotherapy, or sequential balloon placement for sustained weight loss. Studies on the role of exercise in weight loss sustainability following IGB placement are also needed. In addition to efficacy, it will be important to capture the potential for adverse events. Although the risk of serious adverse events appears to be relatively low, early removal due to device intolerance seems to be relatively common. Identifying predictors of device intolerance can help inform patient selection to identify those patients that would be most likely to succeed with IGB therapy.

Indirect evidence suggests that the prophylactic use of concomitant PPI therapy with IGB placement can protect against upper GI bleeding related complications. RCTs that directly assess patient outcomes with PPI use following IGB placement are still needed. Additionally, studies are needed to determine optimal dosing, frequency, and duration of PPI administration. To date, there is a dearth of literature on the use of intraoperative anesthetic regimens and antiemetic regimens both pre- and post-operatively in IGB patients. Given the frequency of nausea reported by patients following IGB placement, this is an important area of research that can help improve IGB tolerance.

Lastly, the micronutrient management of individuals who undergo IGB placement requires additional research. Limited research is available with regards to the need for perioperative laboratory screening for nutritional deficiencies or micronutrient needs following IGB placement. Ultimately, more research is needed to determine the optimal protocol for IGB placement, maintenance, and sustainability of metabolic improvements. There are several limitations associated with these recommendations. Some of recommendations are based heavily on indirect or imprecise evidence at this time due to the limited literature available. In particular, recommendations on micronutrient monitoring and management of IGB placement as well as subsequent weight loss or maintenance interventions following removal all received conditional recommendations with low to very low certainty. Therefore, it is distinctly possible that future research may alter future recommendations regarding IGB therapy in the management of obesity.

In conclusion, the AGA suggests IGB therapy with moderate to high intensity lifestyle therapy as a weight loss intervention over lifestyle intervention alone. In addition, the AGA recommends concomitant treatment with PPI therapy. In the context of limited evidence, the AGA suggests using the intraoperative anesthetic regimens associated with the lowest incidence of nausea and a scheduled antiemetic regimen for two weeks after IGB placement. Additionally, the AGA recommends against perioperative laboratory screening for nutritional deficiencies, but does suggest 1-2 multivitamins after IGB placement. After IGB removal, the AGA recommends subsequent weight loss or maintenance interventions that include dietary interventions, pharmacotherapy, repeat IGB, or bariatric surgery and that a strategy be determined based on a shared decision-making approach. The AGA recognizes that new evidence may emerge in the future that might strengthen or modify some of the recommendations for the use of IGB in management of obesity.

Plans for Updating This Guideline:

Guidelines are living products. To remain useful, they need to be updated regularly as new information accumulates. This document will be updated when major new research is published. The need for update will be determined no later than in 2022.

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Table 1: Interpretation of the certainty in evidence of effects using the GRADE framework

High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very Low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect

Table 2 : Interpretation of strong and conditional recommendations using the GRADE framework

Implications	**Strong recommendation**	**Conditional recommendation**
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Different choices will be appropriate for individual patients consistent with his or her values and preferences. Use shared-decision making. Decision aids may be useful in helping patients make decisions consistent with their individual risks, values and preferences.
For policy makers	The recommendation can be adapted as policy or performance measure in most situations	Policy making will require substantial debate and involvement of various stakeholders. Performance measures should assess whether decision making is appropriate.
* Strong recommendations are indicated by statements that lead with “we recommend”, while conditional recommendations are indicated by statements that lead with “we suggest”		

Table 3 : AGA recommendations on intragastric balloon therapy in the management of obesity

Statement	Strength of recommendation	Quality of evidence
1. In obese individuals seeking a weight loss intervention, AGA suggests the use of IGB therapy with life style modification over life style modification alone.[a]	Conditional	Moderate
2. In obese individuals undergoing IGB therapy, AGA recommends moderate to high intensity concomitant life style modification interventions to maintain and augment weight loss	Strong	Moderate
3. In individuals undergoing IGB therapy, AGA recommends concomitant treatment with proton pump inhibitors	Strong	Moderate
4. In individuals undergoing IGB therapy, AGA suggests using the intraoperative anesthetic regimens associated with the lowest incidence of nausea along with perioperative antiemetics. AGA suggests a scheduled antiemetic regimen for 2 weeks after IGB placement. [b]	Conditional	Low
5. In individuals undergoing IGB therapy, AGA suggests against perioperative laboratory screening for nutritional deficiencies	Conditional	Low
6. AGA suggests 1-2 multivitamins after IGB placement	Conditional	Very low
7. After IGB removal, AGA suggests subsequent weight loss or maintenance interventions that include dietary interventions, pharmacotherapy, repeat IGB or bariatric surgery. The choice of weight loss or maintenance method after IGB is determined based on patient's context and comorbidities following a shared decision-making approach	Conditional	Low

[a] *Implementation remark:* Fluid filled balloons may be associated with higher efficacy and lower tolerability than air fluid balloons. A shared decision making is suggested for determining device choice.

[b] *Implementation remark:* Evidence is insufficient to recommend a specific antiemetic regimen. The choice of regimen is based on institutional policy, clinical context and availability.