



# Impact of glucagon-like peptide receptor agonists on endoscopy and its preoperative management: Guidelines, challenges, and future directions

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## Abstract

Glucagon-like peptide receptor agonists (GLP-1RA) are used to treat type 2 diabetes mellitus and, more recently, have garnered attention for their effectiveness in promoting weight loss. They have been associated with several gastrointestinal adverse effects, including nausea and vomiting. These side effects are presumed to be due to increased residual gastric contents. Given the potential risk of aspiration and based on limited data, the American Society of Anesthesiologists updated the guidelines concerning the preoperative management of patients on GLP-1RA in 2023. They included the duration of mandated cessation of GLP-1RA before sedation and usage of "full stomach" precautions if these medications were not appropriately held before the procedure. This has led to additional challenges, such as extended waiting time, higher costs, and increased risk for patients. In this editorial, we review the current societal guidelines, clinical practice, and future directions regarding the usage of GLP-1RA in patients undergoing an endoscopic procedure.

**Key Words:** Glucagon-like peptide receptor agonists; Endoscopy; Adverse events; Intubation; Aspiration; Semaglutide; Healthcare burden; Guidelines

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**Core Tip:** Glucagon-like peptide-1 receptor agonists can cause delay in gastric emptying. While the American Society of Anesthesiologists recommend holding these medications prior to all procedures, the American Gastroenterological Association recommends individualized approach prior to endoscopy due to inconclusive clinical data.

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## INTRODUCTION

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are approved for treating diabetes mellitus (DM) and obesity[1-3]. These medications stimulate insulin secretion, which improves glucose control and delays gastric emptying. The exact mechanism by which GLP-1RA affects gastrointestinal motility is not fully understood, but it appears to be neurally mediated. GLP-1RA has been shown to inhibit gastropancreatic function by interfering with central parasympathetic outflow. Gastrointestinal adverse events are common with GLP-1RAs, such as nausea and vomiting, with an increased risk of gastroparesis, pancreatitis, and bowel obstruction[4,5]. However, the favorable use profile of GLP-1RAs is evident in their rapidly increasing adoption[6].

One of the upcoming implications of GLP-1RAs is their effect on gastric emptying in the perioperative period[7-10]. Despite the standard fasting duration, patients on GLP-1RAs are reported to have high amounts of residual gastric content, increasing the risk of intraoperative aspiration[8]. In addition to the delayed gastric emptying, GLP-1RAs also reduce duodenal and small intestine motility, with variable effect depending on the presence or absence of diabetic neuropathy associated dysautonomia[11]. Furthermore, the observed rate of aspiration during upper gastrointestinal endoscopies in patients on GLP-1RAs has been low in the clinical studies[12,13]. Regardless, the recent American Society of Anesthesiologists (ASA) guideline recommends holding GLP-1RAs either on the day of the procedure (for daily dosing) or a week prior to the procedure (for weekly dosing)[14-16]. On the contrary, gastrointestinal societies have recommended individualized approaches when considering endoscopy in this subset of patients[17,18]. In the following editorial, we review the current societal guidelines, clinical practice, and future directions regarding the usage of GLP-1RAs in patients undergoing an endoscopic procedure.

## CURRENT EVIDENCE

In a recent single center retrospective study by Silveira *et al*[8], the effect of perioperative semaglutide use on residual gastric content was assessed in patients undergoing upper endoscopy[8]. A significantly higher number of patients on semaglutide were found to have increased residual gastric content as compared to the control group (24.2% *vs* 5.1%). Interestingly, patients with and without increased residual gastric content had similar time of preoperative semaglutide interruption (around 10 d). Furthermore, no correlation was found between semaglutide use and the 'amount' of residual gastric content. Only 1 out of 33 patients on semaglutide reported to have pulmonary aspiration. It is worthwhile noting that semaglutide had these effects despite the patients having an average fasting interval of 9.3 h (clear fluids) and 14.5 h (solids), which is longer than the recommended fasting periods[19]. The findings of this study were replicated in case reports and another matched pair case-control study with higher incidence of gastric residue in patients taking GLP-1RAs (5.4% *vs* 0.49%)[10,20].

In addition to upper endoscopy, the delayed gastrointestinal motility observed with GLP-1RAs affects bowel preparation during colonoscopy as well[21]. In a retrospective case-control study of 333 patients, the Boston Bowel Preparation Scale was noted to be numerically lower in patients on GLP-1RAs[21]. An important point to consider, however, was the significantly higher number of patients with diabetes in the GLP-1RA group, which can itself cause suboptimal bowel preparation[22].

Not all the evidence implicates GLP-1RAs as a negative predictor of outcomes in patients undergoing endoscopies. In a retrospective cohort study with matched controls, Stark *et al*[13] found no significant difference in retained food on upper endoscopy between patients treated with and without GLP-1RAs (95%CI: 0.87-20.34)[13]. Additionally, the correlation of residual gastric content with actual pulmonary aspiration events remains unclear. Anazco *et al*[12] reported only 2 cases of pulmonary aspiration among 4134 endoscopies in patients on GLP-1RAs, equivalent to a rate of 4.8 events per 10000 endoscopies[12]. This is similar to the previously reported overall rate of 4.6 aspiration events per 10000 endoscopies, irrespective of the type of medications or comorbidities[23]. Nevertheless, the effect of GLP-1RAs in the perioperative period continues to be explored as it pertains to procedures other than endoscopies as well[24,25].

## GUIDELINES

The ASA Task Force on Preoperative Fasting released the following recommendations for patients on GLP-1RAs: (1) For urgent or emergent procedures, the patients are to be managed as if they are 'full stomach'; (2) For elective procedures, GLP-1RAs are to be held either on the day of the procedure (for daily dosing) or a week prior to the procedure (for weekly dosing); (3) These guidelines are suggested irrespective of the dose/indication for GLP-1RAs and the type of procedure; and (4) If the GLP-1RAs were not held as advised for elective procedures, then the patients are to be considered 'full stomach'[14].

Immediately after the release of ASA recommendations, a multi-society statement was released by American Gastroenterological Association, American Association for the Study of Liver Diseases, American College of Gastroenterology, American Society for Gastrointestinal Endoscopy, and North American Society For Pediatric Gastroenterology, Hepatology & Nutrition[26]. Given the conflicting results from clinical studies regarding the risk of aspiration and gastroparesis due to GLP-1RAs, along with the possibility of such effects being dose or indication dependent, the societies concluded that there is insufficient data to support stopping GLP-1RAs before elective endoscopy.

Hence, an individualized approach was advised based on the patient factors such as indication for taking GLP-1RAs, whether symptomatic, urgency of the endoscopy, and whether the standard fasting period was observed[17]. First, a single dose of GLP-1RAs could be held if the indication for use is weight loss, although it is unclear if the gastric motility will improve on holding a single dose. On the contrary, if the GLP-1RA is being prescribed for DM, holding it can expose the patient to the risk of hyperglycemia, which can itself lead to adverse procedural outcomes[27]. Second, transabdominal ultrasonography can be performed in symptomatic patients with suspected residual gastric content[28]. Third, rapid-sequence intubation can be considered in symptomatic patients where endoscopy cannot be delayed. Fourth, instead of stopping GLP-1RAs, the patients can be placed on liquid diet on the day before the procedure, especially as a prior study showed protective effect of combined upper and lower endoscopies against residual gastric content likely due to consumption of liquid diet the day prior[8].

## CLINICAL IMPLICATIONS

The differences in recommendations between ASA and gastroenterology societies have a potential to impact clinical decision making in patients needing endoscopies. As such, the use of GLP-1RAs has been less persistent in DM/obese patients in real world studies[29]. Adding to that, stopping GLP-1RAs regardless of the type of procedure may cause more harm than benefit by causing poor glucose control and averting the cardioprotective benefits of GLP-1RAs. There are many factors that need to be considered when interpreting the currently available evidence: (1) Acetaminophen absorption test has been used in many studies for measuring gastric emptying. However, it is not the gold standard and is not reliable; (2) long-acting GLP-1RAs affect gastric motility less than short-acting GLP-1RAs; and (3) possible tachyphylaxis exists with GLP-1RAs as the effect on gastric motility decreases with increasing dose or duration[16,30,31].

## CONCLUSION

In conclusion, managing GLP-1RAs in the perioperative period may not be as simple as other non-insulin glucose-lowering agents. While the ASA guidelines may hold true for other procedures/surgeries regarding holding of GLP-1RAs, the same may not apply to endoscopies given the lack of conclusive data and different levels of sedation required in various procedures. We concur with the statement by gastroenterology societies in terms of an individualized approach to GLP-1RAs before endoscopies. This may change with time as newer and larger studies become available in the future assessing the direct impact of perioperative use of GLP-1RAs on patient outcomes.

## FOOTNOTES

**Author contributions:** Singh S and Suresh Kumar VC contributed equally to this paper; Suresh Kumar VC and Aswath G designed the overall concept and outline of the manuscript; Singh S contributed to the discussion and design of the manuscript; Singh S and Suresh Kumar VC contributed to the writing, and editing the manuscript, illustrations, and review of literature; Aswath G contributed to the writing and editing of the manuscript.

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