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GLP-1 Receptor Agonists and Perioperative Aspiration Risk: Reconciling Residual Gastric Content with Clinical Outcomes - A Narrative Review

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Abstract

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly prescribed for type 2 diabetes and obesity, but their effect of slowing gastric emptying may leave patients with higher residual gastric content (RGC) at the time of elective procedures, raising concern among anesthesiologists for pulmonary aspiration. This narrative review synthesizes evidence on the physiologic mechanisms, perioperative outcomes, and clinical guidance surrounding GLP-1 RA use. Using PubMed and Scopus, we reviewed English-language studies published from 2020 through 2026 and professional society guidance on gastric physiology, aspiration risk, and perioperative outcomes in patients receiving GLP-1 RAs. Findings were synthesized narratively, distinguishing physiologic measures of gastric emptying and RGC from clinically confirmed pulmonary aspiration. The available evidence largely associates GLP-1 RA use with delayed gastric emptying and increased RGC despite standard fasting. However, large observational cohorts have not shown a corresponding rise in pulmonary aspiration. RGC also appeared more prevalent with weight-loss than glycemic-control use, although this comparison is confounded by dose and patient characteristics. Effects on gastric emptying may attenuate with prolonged therapy, but recent dosing remains associated with higher RGC. Considering this uncertainty, guidance has shifted from routine discontinuation toward individualized, risk-stratified management, although international recommendations continue to differ. Overall, aspiration risk in patients receiving GLP-1 RAs appears multifactorial rather than attributable to drug exposure alone, thereby not supporting uniform discontinuation prior to procedures. Instead, individualized risk assessment should consider treatment phase, gastrointestinal symptoms, and comorbidities, with point-of-care gastric ultrasound as an adjunct where available. Such an approach may better guide management until outcome-based evidence emerges.

Keywords: Aspiration; GLP-1R agonist; Obesity; Perioperative anesthesia; Pulmonary complications; Regurgitation; Residual gastric content; Tachyphylaxis

Introduction

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) were initially developed for the treatment of type 2 diabetes mellitus but have since emerged as effective pharmacologic therapies for long-term weight management in obesity [1-3]. This expanded role was reinforced by the Semaglutide Treatment Effect in People with obesity (STEP) program, which led to FDA approval of once-weekly 2.4 mg subcutaneous semaglutide injections for chronic weight management in April 2021 [4]. Beyond their ability to control blood glucose and influence body weight, GLP-1 RAs offer additional cardiometabolic benefits and have been shown to significantly reduce major adverse cardiovascular events in

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high-risk individuals [5-8]. Multiple large cardiovascular outcome trials have consistently suggested that GLP-1 RAs significantly reduce major adverse cardiovascular events and cardiovascular outcomes, including hospitalizations for heart failure [9]. As a result, these additional clinical benefits have contributed to a rapid rise in GLP-1 RA use across diverse patient populations in the United States [1]. In a retrospective cohort analysis of adults living in the United States with type 2 diabetes, the percentage treated with a GLP-1 RA increased from 3.2% in 2015 to 10.7% in 2019 [10]. Therefore, the increased use of GLP-1 RAs represents an important clinical consideration for anesthesiologists, given their ability to delay gastric emptying, which has raised concern for pulmonary aspiration under anesthesia [11]. As the use of GLP-1 RAs continues to expand, attention has increasingly turned to their perioperative implications, particularly those relevant to anesthetic safety. GLP-1 RAs have been shown to delay gastric emptying, leading to increased residual gastric content (RGC) prior to elective procedures despite adherence to standard preoperative fasting guidelines [1] [10-13]. Also, it is critical to manage other potential complications due to anesthesia [14-21]. This leads to concerns for elevated pulmonary aspiration risk under anesthesia, which has prompted anesthesiology societies to issue new perioperative guidelines to mitigate aspiration risk [22]. In a prospective observational study using preoperative point-of-care gastric ultrasonography, GLP-1 RA use was associated with an increased RGC, particularly when the medication was withheld for shorter durations prior to surgery [23]. This finding raises concerns about the adequacy of standard fasting guidelines for patients taking GLP-1 RAs, as increased RGC may persist despite prolonged fasting durations [23]. However, large cohort studies have not observed a higher incidence of postoperative aspiration pneumonia among patients taking GLP-1 RAs compared to nonusers [24]. At the same time, conservative discontinuation of GLP-1 RAs days to weeks before surgery may unnecessarily forfeit glycemic control and weight management benefits without clear evidence of improved safety outcomes. Therefore, there is a critical need to better understand how perioperative fasting guidelines and anesthetic care should be tailored to patients taking GLP-1 RAs. This review examines the established physiologic effects of GLP-1 RAs, such as delayed gastric emptying and increased gastric volumes, and relates them to emerging perioperative outcomes in humans. Understanding these physiologic effects requires consideration of the underlying pharmacologic properties of GLP-1 RAs, as differences in drug structure directly influence duration of action and systemic exposure. Structural modifications, including amino acid substitutions, fatty acid conjugation, and fusion with carrier molecules, are applied to GLP-1 RAs to minimize metabolism and renal excretion, thereby allowing for prolonged half-lives and sustained pharmacological effects [25]. Therefore, understanding how the pharmacologic properties of GLP-1 RAs affect gastrointestinal physiology is essential for interpreting aspiration risk markers and predicting adverse perioperative outcomes. However, pulmonary aspiration in patients taking GLP-1 RAs appears to be rare, highlighting a discrepancy between risk indicators and observed clinical outcomes [26]. Retained gastric contents have been observed more frequently among GLP-1 RA users during endoscopy; however, these findings have rarely translated into clinically significant pulmonary aspiration events, highlighting translational limitations of existing data [27-29]. Throughout this review, we therefore distinguish between successive steps in a proposed pathway: delayed gastric emptying, increased RGC, regurgitation, pulmonary aspiration, and clinically significant pulmonary complications. Since evidence is strongest for the earliest steps and weakest for clinical outcomes, increased RGC is treated as a surrogate marker of potential aspiration risk rather than as evidence of aspiration itself. This review emphasizes the importance of anesthesia-specific risk assessment, as patients with gastrointestinal symptoms or recent GLP-1 RA use may warrant closer perioperative evaluation and more individualized management. Unlike prior reviews, this review explicitly separates surrogate gastric findings from clinically confirmed aspiration outcomes and traces the chronological evolution of professional society guidance, with the aim of clarifying why current recommendations diverge.

Methods

This narrative review evaluates the perioperative implications of GLP-1 RA therapy during anesthesia and procedural sedation. Given the heterogeneity of the available studies, findings were synthesized narratively rather than pooled quantitatively. Search terms and inclusion and exclusion criteria were defined to identify studies assessing how GLP-1 RA use influences gastric physiology, aspiration risk, and clinical outcomes in perioperative and procedural settings. Articles were selected based on their analysis of patients receiving GLP-1 RA therapy and their evaluation of gastric emptying, RGC, pulmonary aspiration, regurgitation, perioperative fasting, airway management, or anesthesia-related outcomes. Priority was given to studies that used validated measures of gastric function, such as point-of-care gastric ultrasonography, gastric scintigraphy, or acetaminophen absorption testing, as well as those that evaluated aspiration risk, retained gastric contents, or perioperative safety in patients receiving GLP-1 RAs. Studies that did not involve patients receiving GLP-1 RA therapy, or that did not specifically analyze gastric motility, aspiration risk, or related perioperative outcomes, were excluded. The literature search was conducted using PubMed and Scopus. Each search query was constructed from a combination of three sets of keywords. The first set includes terms identifying the drug class: "glucagon-like peptide-1 receptor agonist,"

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"GLP-1 receptor agonist," "GLP-1 RA," "semaglutide," "liraglutide," "dulaglutide," "tirzepatide," OR "exenatide." The second set specifies the perioperative or procedural context with the keywords "perioperative," "preoperative," "anesthesia," "anaesthesia," "sedation," "endoscopy," "surgery," OR "procedural." The third set specifies outcomes relevant to anesthetic safety, including the keywords "gastric emptying," "gastric content," "residual gastric content," "pulmonary aspiration," "aspiration," "regurgitation," "fasting," "airway management," OR "aspiration pneumonia." The review was limited to English-language studies published between 2020 and 2026, with earlier foundational studies on pharmacology and gastric motility included when relevant to the mechanistic framework of the review. Titles and abstracts were screened by three authors (K.G.V., H.M., and N.N.), and full texts of potentially relevant articles were reviewed for eligibility. Reference lists of included articles were also reviewed for additional studies, and perioperative guidance documents were identified from relevant professional society websites. Evidence was organized according to an outcome hierarchy, distinguishing gastric emptying, residual gastric content, regurgitation, and clinically confirmed pulmonary aspiration. Formal risk-of-bias assessment was not performed; instead, study design and major sources of bias are noted where relevant.

Pharmacologic and Physiologic Relevance to Anesthesia

GLP-1 Receptor Agonist Classes and Dosing Patterns

GLP-1 RAs delay gastric emptying by acting on both central and peripheral pathways, including vagal-mediated suppression of gastric motility and enteric-mediated increases in pyloric tone (Figure 1). Across perioperative and procedural patient populations, the use of GLP-1 RAs has been frequently associated with delayed gastric emptying as reflected by increased RGC despite adherence to standard fasting protocols [30]. Evidence from endoscopy and anesthesia-based studies demonstrates that this pattern occurs with varying dosing strategies, although the frequency and magnitude may vary with treatment phase and timing of the last dose.

GLP-1 receptor agonist administration activates GLP-1 receptors, triggering two parallel pathways: a central (vagal-mediated) pathway that suppresses gastric motility, and a peripheral (enteric-mediated) pathway that increases pyloric tone. Both lead to delayed gastric emptying, which drives metabolic effects (increased insulin secretion, decreased glucagon release, and increased satiety) and leads to perioperative concerns (increased retained gastric content and uncertain aspiration risk). Created in https://BioRender.com. Among patients receiving GLP-1 RA therapy, observational endoscopy studies have reported a higher prevalence of RGC at the time of the procedure

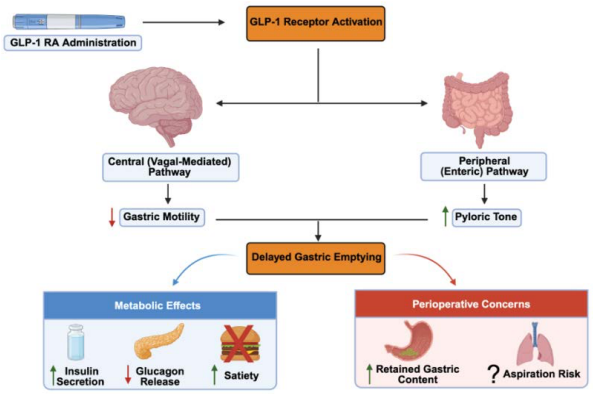


Figure 1: Mechanisms of GLP-1 Receptor Agonists.

compared with patients not receiving GLP-1 therapy [26]. In fasting ultrasound-based assessments, GLP-1 RA use was similarly associated with retained solid or liquid gastric contents despite standard fasting intervals [31,32]. Several case reports have also described intraoperative regurgitation and pulmonary aspiration events in patients using long-acting GLP-1 RAs who otherwise met conventional fasting criteria [33,34], although case reports cannot establish causation or event frequency. Long-acting weekly GLP-1 RAs have been evaluated in multiple gastric ultrasound and perioperative anesthesia cohorts. In these studies, weekly semaglutide use was associated with increased residual gastric volume and a higher prevalence of retained gastric contents at the time of elective procedures compared with non-GLP-1 RA users [1]. In a prospective study of surgical patients, semaglutide use within 10 days of surgery was associated with an increased RGC on preoperative point-of-care gastric ultrasound when compared with non-GLP-1 RA users [35]. Dual incretin agonists such as tirzepatide, which target both GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptors, have emerged as a newer class of glucose-lowering agents, although data evaluating their use in the perioperative setting remain limited. In periprocedural studies that included patients receiving dual GLP-1 and GIP RAs, findings related to delayed gastric emptying, including retained gastric contents, were similar to those observed in patients receiving GLP-1 RAs alone [27]. In large observational cohorts assessing postoperative pulmonary outcomes, dual agonist use grouped with GLP-1 RA therapy was not associated with an increased incidence of aspiration pneumonia compared with nonusers [24]. Given these similar findings, tirzepatide is included within the term GLP-1 RA throughout this review, with tirzepatide-specific findings identified where reported.

Retained Gastric Content in GLP-1 Receptor Agonist Therapy

The perioperative studies evaluating GLP-1 RA use did not directly measure gastric motor physiology but instead

assessed delayed gastric emptying indirectly through RGC identified by ultrasound or endoscopic visualization. Collectively, these studies suggest delayed gastric emptying based on the presence of solid or liquid gastric contents despite fasting for intervals that are considered adequate under current anesthesia guidelines. Several clinical studies reported increased gastric volumes in GLP-1 RA users despite standard fasting, likely attributable to impaired gastric clearance and delayed gastric emptying [21,26]. These findings were reported in both anesthesia and endoscopy-based cohorts and did not appear to be explained by differences in fasting duration or dietary noncompliance. Preprocedural gastric ultrasound studies further supported these findings by demonstrating retained solid material in GLP-1 RA users, suggesting delayed clearance of solids from the stomach [31]. Endoscopic evaluations have similarly described solid food retention in patients receiving GLP-1 RAs at the time of elective procedures [26,37,38]. Consistent with these findings, semaglutide use was associated with higher rates of retained gastric contents during upper endoscopy compared with matched controls, with patients using semaglutide for weight loss demonstrating a greater risk of retained contents than those using it for glycemic control [39]. Retention of liquid gastric contents was also observed, with ultrasound-based assessments identifying increased gastric volume following clear liquid fasting in patients receiving GLP-1 RAs, indicating delayed gastric outflow rather than fasting noncompliance [31]. A separate study additionally identified liquid retention in patients receiving GLP-1 RA therapy and interpreted this finding as consistent with delayed gastric emptying [1]. Across studies, substantial interpatient variability was observed in the presence and volume of RGC among GLP-1 RA users. Findings varied between patients, with some demonstrating empty stomachs despite recent dosing, while others exhibited significant retained gastric contents under similar fasting conditions [1,35]. In large population-based analyses evaluating postoperative aspiration pneumonia, GLP-1 RA use was not associated with an increased incidence of aspiration events, indicating that delayed gastric emptying does not uniformly translate into clinical aspiration outcomes [24, 40-42].

Tachyphylaxis and Treatment-Phase Effects of GLP-1 Receptor Agonists

The early treatment and dose escalation phases represent a distinct period during GLP-1 RA therapy, during which pharmacologic exposure and physiologic effects may differ from those seen with stable long-term use. In a phase 1, 4-week study, once-weekly tirzepatide delayed gastric emptying after a single dose, with a reduced effect observed after repeated dosing of tirzepatide or dulaglutide [43]. In a double-blind, parallel-group trial in adults with obesity, gastric emptying was assessed during dose-escalated semaglutide therapy using paracetamol absorption. In this trial, semaglutide therapy was associated with a significant reduction in the rate of gastric emptying during the early dose escalation phase, whereas this effect was no longer observed after prolonged treatment at week 20 [44]. In a longitudinal study of liraglutide, a once daily GLP-1 RA, delayed gastric emptying was observed in 57% of participants at 5 weeks and in 30% of participants at 16 weeks, which was consistent with the development of tachyphylaxis during chronic treatment [45]. Despite evidence of attenuation with continued GLP-1 RA therapy, recent semaglutide exposure in the perioperative setting remains associated with retained gastric contents at the time of elective surgery. In a prospective population assessed with preoperative gastric ultrasound, increased RGC was observed in 40% of patients who had received semaglutide within 10 days of surgery compared with 3% of nonusers [45]. Preoperative interruption of semaglutide use within 10 days was associated with increased RGC, and earlier discontinuation of semaglutide therapy did not result in reduced retained gastric contents [35,45]. These findings suggest that, although the effects of GLP-1 RAs may attenuate over time, they can still affect gastric emptying in the perioperative setting, particularly with recent use.

Gastric Emptying Measures in GLP-1 Receptor Agonist Trials

In randomized controlled trials, GLP-1 RAs have been studied for their effects on gastric emptying using physiologic measures such as gastric scintigraphy and acetaminophen absorption testing. In one randomized placebo-controlled trial, gastric emptying was assessed using gastric scintigraphy after ingestion of a standardized solid meal, with imaging performed at intervals over a four-hour period to quantify gastric retention [46]. Semaglutide treatment was associated with greater proportions of retained gastric contents at each time point and a prolonged median gastric emptying half-time when compared with placebo. These findings reflect delayed gastric emptying throughout the observation period [46]. Comparable scintigraphic assessments have been applied in randomized placebo-controlled trials of liraglutide. In a 16-week randomized trial in adults with obesity, liraglutide was dose-escalated to 3.0 mg daily, which significantly prolonged the gastric emptying half-time of solids at both 5 weeks, and 16 weeks compared with placebo [47]. Acetaminophen absorption has also been used as an indirect measure of gastric emptying in randomized trials. In a 20-week double-blind trial in adults with obesity, once-weekly semaglutide (2.4 mg) increased the total acetaminophen absorbed over 5 hours compared with placebo, with no evidence of delayed gastric emptying at week 20 [44]. Similarly, in a randomized placebo-controlled trial of oral semaglutide dose escalated to 50 mg daily for 20 weeks, an acetaminophen-based assessment showed no statistically significant difference in gastric emptying at the end of the study when compared with placebo [48].

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Perioperative and Anesthesia-Specific Clinical Evidence

Perioperative Gastric Ultrasonography: Assessment of Gastric Contents and Clinical Utility

Recent perioperative investigations have evaluated whether GLP-1 RA therapy is associated with delayed gastric emptying as detected by point-of-care gastric ultrasonography. A prospective observational study of volunteers who recently started on semaglutide demonstrated a higher prevalence of residual solid gastric contents on gastric ultrasound after an overnight fast compared with controls, with differences persisting after ingestion of clear liquids [31]. In a prospective cross-sectional study of patients presenting for elective procedures under anesthesia, GLP-1 RA use was associated with increased RGC detected by preprocedural gastric ultrasonography despite adherence to standard fasting guidelines [1]. These findings are supported by additional perioperative observational data demonstrating an association between GLP-1 RA use and increased RGC at the time of elective procedures [35]. In a multicenter observational study of patients undergoing anesthesia, a substantial proportion of patients receiving GLP-1 RAs met criteria for high RGC, defined by the presence of solid contents or increased gastric fluid volume on preoperative ultrasonography [23]. In contrast, a separate prospective observational study of fasting surgical patients found no significant difference in estimated gastric volume between those receiving GLP-1 RAs and those not receiving them, as assessed by gastric ultrasonography [49]. Several studies have evaluated the performance of gastric ultrasonography for assessing gastric content and estimating gastric volume in perioperative and procedural settings. In a prospective noninferiority study of fasted elective surgical patients, baseline gastric volume was not higher in diabetic than in nondiabetic patients, and the frequency of a full stomach was also similar between groups, suggesting that gastric ultrasound assessment is applicable in diabetic patients following standard fasting instructions [50]. Similarly, in a multicenter study of adults undergoing gastroscopy under intravenous anesthesia, gastric volume measured by endoscopic aspiration immediately after ultrasonography was used to develop and validate predictive models based on age, Perlas grade, and right lateral decubitus antral cross-sectional area, which showed better agreement with observed gastric volume than the traditional Perlas model [51]. In a separate study evaluating point-of-care gastric ultrasound against reported fasting duration, estimated gastric volume showed only a weak inverse correlation with fasting duration, supporting the role of ultrasound in individualized assessment rather than reliance on fasting history alone [52]. Collectively, these studies support the feasibility of qualitative grading and quantitative antral cross-sectional area-based approaches for estimating gastric content and gastric volume in patients undergoing anesthesia or procedural sedation. Alongside upper endoscopy, gastric scintigraphy, and the acetaminophen absorption test, gastric ultrasonography offers a complementary bedside approach for assessing gastric content, with each method carrying distinct strengths and limitations

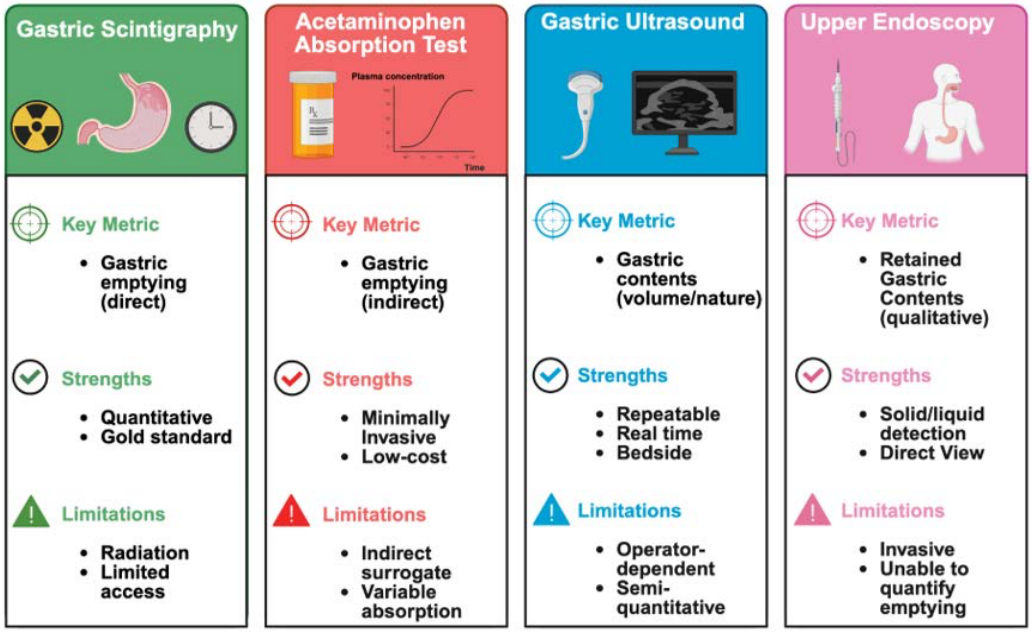


Figure 2: Techniques Used to Evaluate Gastric Emptying and Gastric Contents.

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Four techniques are compared by key metric, strengths, and limitations: gastric scintigraphy, acetaminophen absorption test, gastric ultrasound, and upper endoscopy. Created in https://BioRender.com. Recent investigations have further evaluated the reproducibility of gastric ultrasonography measurements and the training required for clinicians to achieve competency in perioperative practice. In a study of critically ill patients receiving enteral nutrition, qualitative and quantitative ultrasound assessments of gastric content demonstrated good intraobserver and interobserver agreement, supporting the reliability of both antral grading and volume estimation techniques [53]. In parallel, perioperative studies of operator performance have characterized the learning curve associated with gastric ultrasonography, demonstrating that scan duration decreases with experience and that performance stabilizes after repeated examinations [54]. In this context, structured training programs with supervised examinations have been shown to enable clinicians to perform gastric ultrasound efficiently in clinical settings, although variability in scan difficulty may persist based on patient-related factors [54]. These findings support gastric ultrasonography as a reproducible technique that can be incorporated into perioperative risk assessment with appropriate training and experience. However, its use has practical limitations. Achieving competency requires structured training, and image acquisition may be technically difficult or inconclusive in some patients, particularly those with obesity [54,83]. Access to equipment and trained personnel can also vary across clinical settings. More importantly, while gastric ultrasound can identify gastric contents, it has not been shown to reduce pulmonary aspiration or improve clinical outcomes, and RGC has not been validated against aspiration events. Therefore, gastric ultrasound is best viewed as an adjunct to clinical judgment rather than a definitive measure of aspiration risk.

Aspiration, Regurgitation, and Pulmonary Complications

Early perioperative evidence describing aspiration and regurgitation events in patients receiving GLP-1 RAs has largely come through case reports and small case series, with repeated observations of retained gastric contents despite adherence to standard fasting guidelines. A case report described intraoperative pulmonary aspiration in a patient receiving semaglutide for weight loss, in whom substantial gastric contents were identified despite prolonged fasting and required bronchoscopic removal [34]. In a separate report, regurgitation of a large volume of gastric contents occurred during induction of general anesthesia in a patient taking semaglutide despite prolonged preoperative fasting and without traditional risk factors [33]. Similar findings have been reported in small case series, including particulate gastric contents and regurgitation events in patients receiving GLP-1 RAs despite appropriate fasting [55]. Additional case series in elective surgical patients have demonstrated retained solid gastric contents on preoperative gastric ultrasonography following prolonged fasting, resulting in procedure postponement due to concern for aspiration risk [56]. Large retrospective cohort studies have primarily evaluated whether GLP-1 RA use is associated with retained gastric contents and whether this is associated with a higher frequency of aspiration-related events. A historical cohort study of fasting patients undergoing endoscopy under anesthesia care reported visible gastric contents in 19% of procedures in the GLP-1 RA group compared with 5% in controls, with one case of pulmonary aspiration observed in the GLP-1 RA group and none in controls [57]. In contrast, a large comparative cohort study of over 43,000 adults with type 2 diabetes undergoing upper gastrointestinal endoscopy found that GLP-1 RA use within 30 days of the procedure was not associated with an increased risk of pulmonary aspiration compared with sodium-glucose cotransporter 2 inhibitor use, with event rates of 4.15 versus 4.26 per 1,000 individuals, respectively [58]. The same study demonstrated that GLP-1 RA use was associated with a higher risk of endoscopy discontinuation, with a pooled risk ratio of 1.99, suggesting a possible association with retained gastric contents despite the absence of increased aspiration events [58]. Collectively, these findings suggest that while GLP-1 RA use is frequently associated with increased retained gastric contents, this has not translated into a clearly increased incidence of pulmonary aspiration in larger cohort studies, although procedural disruptions may occur. Figure 3 summarizes this discrepancy between a surrogate marker (RGC) and clinical outcomes (aspiration), which recurs as a central theme throughout the perioperative GLP-1 RA literature.

Under normal conditions, gastric motility and pyloric relaxation allow timely emptying with minimal RGC after standard fasting, whereas GLP-1 RA use is associated with reduced motility and increased pyloric tone, resulting in delayed emptying and higher RGC despite fasting, raising theoretical concern for aspiration risk. Created in https://BioRender.com.

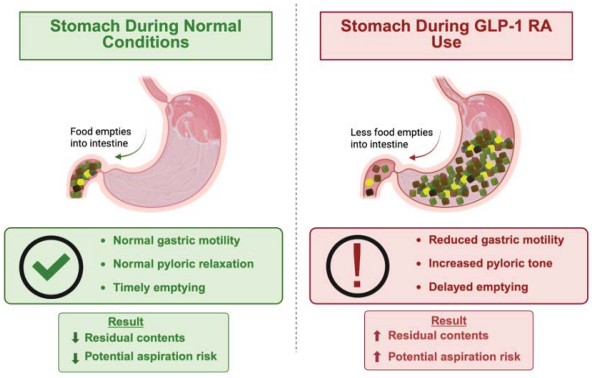


Figure 3: Comparison of Gastric Emptying in Normal Conditions versus during GLP-1 Receptor Agonist Use.

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Several observational studies have evaluated whether GLP-1 RA use is associated with an increased risk of aspiration or pulmonary complications and have not demonstrated such a risk [59]. A nationwide retrospective cohort study of patients with type 2 diabetes undergoing outpatient upper endoscopy reported that pulmonary adverse events, including aspiration, aspiration pneumonia, pneumonia, and respiratory failure, were rare and not increased among patients receiving GLP-1 RAs compared with dipeptidyl peptidase-4 inhibitor users [60]. Additionally, a retrospective cohort study of 13,523 patients undergoing esophagogastroduodenoscopy or colonoscopy found no aspiration events among GLP-1 RA users and no independent association between GLP-1 RA therapy and aspiration-related diagnoses within 30 days of the procedure [61]. Beyond endoscopic settings, retrospective studies in large surgical cohorts have similarly found no significant increase in aspiration risk or major perioperative complications among GLP-1 RA users, further supporting the low incidence of aspiration observed across diverse procedural settings [62,63]. In a cohort of patients undergoing upper endoscopy under anesthesia, individuals receiving GLP-1 RAs demonstrated higher rates of diabetes, increased American Society of Anesthesiologists (ASA) physical status, and a greater incidence of gastrointestinal symptoms compared with controls, reflecting differences in baseline clinical characteristics between groups [57]. Multivariable analyses adjusting for these factors, including diabetes and fasting duration, did not eliminate the observed association between GLP-1 RA use and RGC. The authors further note that many patients undergoing endoscopy have underlying gastrointestinal conditions that may affect gastric motility. Similarly, large retrospective analyses of perioperative aspiration events demonstrate that pulmonary aspiration most commonly occurs in patients with multiple concurrent risk factors [64]. In a cohort of over 166,000 anesthetic cases, most patients experiencing regurgitation or aspiration had identifiable predisposing conditions, including emergency surgical status and recent oral intake, with emergency procedures showing a strong association with aspiration risk. Additionally, concurrent medications and comorbidities associated with delayed gastric emptying have emerged as a particularly important consideration, as many patients receiving GLP-1 RAs also use agents known to independently impair gastric motility [65]. Within this context, these findings indicate that retained gastric contents and aspiration risk arise from multiple overlapping clinical and physiologic factors rather than a single isolated contributor

Aspiration risk in the perioperative period arises from the combined influence of multiple patient, procedural, and pharmacologic factors: GLP-1 RA therapy, gastrointestinal symptoms, opioid use, obesity, gastrointestinal motility disorders, sedation or anesthetic depth, difficult airway

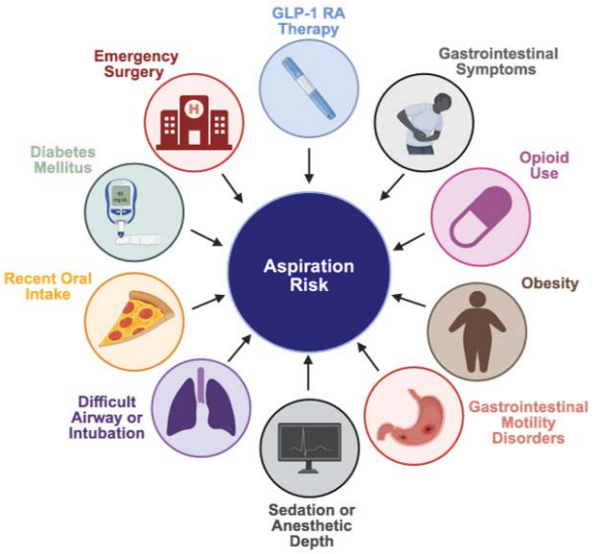


Figure 4: Multifactorial Contributors to Aspiration Risk in the Perioperative Setting.

or intubation, recent oral intake, diabetes mellitus, and emergency surgery. Created in https://BioRender.com. These factors provide a practical basis for preoperative risk stratification. Patients with gastroparesis, bowel dysmotility, or neurological disorders affecting gastric motility appear to be at greatest risk of retained gastric contents and aspiration [70]. Additionally, active gastrointestinal symptoms, including nausea, vomiting, abdominal pain, dyspepsia, or constipation, may further increase risk [60]. Treatment characteristics also contribute, as risk may be higher during the dose-escalation phase, at higher doses, and with weekly formulations [70]. These effects may be compounded by concomitant medications that slow gastric emptying [65], and by emergency surgical status [64]. Although obesity is common among GLP-1 RA users, it should not by itself determine perioperative management [70]. Patients without these features may therefore be managed with standard precautions, whereas those with several risk features may warrant additional measures, such as a preoperative clear-liquid diet, gastric ultrasound, or full-stomach precautions [70,81].

Sedation and Shared-Airway Endoscopic Procedures

Upper endoscopy and related sedation-based procedures represent a clinically relevant setting for aspiration risk due to the use of moderate to deep sedation in a shared airway environment, making this population particularly important for evaluating the perioperative implications of GLP-1 RA use. As noted above, retained gastric contents were more frequent among GLP-1 RA users undergoing endoscopy under anesthesia care [57]. In a multicenter cross-sectional study of patients undergoing endoscopy while prescribed GLP-1 RAs,

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retained gastric contents were reported in 8.7% of cases, with no aspiration events observed and only one patient requiring unplanned intubation [66]. In contrast, a real-world cohort study evaluating continuation of GLP-1 RAs prior to upper endoscopy found no significant differences in retained gastric contents, early termination of procedures, or aspiration events compared with patients who withheld therapy [67]. Taken together, endoscopy-based sedation studies suggest that GLP-1 RA use is associated with increased detection of retained gastric contents, while clinically observed aspiration and pulmonary complications remain uncommon. Observational cohort studies of endoscopic procedures have compared monitored anesthesia care with general anesthesia using a secured airway in patients receiving GLP-1 RAs, with a focus on airway protection during sedation-based techniques. A multicenter retrospective cohort study of outpatient esophagogastroduodenoscopy and colonoscopy reported no aspiration events in either GLP-1 RA users or nonusers [68]. In analyses comparing these techniques among GLP-1 RA users, monitored anesthesia care or moderate sedation was associated with higher odds of hospitalization compared with general anesthesia, while other clinical outcomes did not differ between groups. A single-center retrospective cohort study of outpatient upper endoscopy similarly reported no cases of pulmonary aspiration and found no significant differences in hypoxic events between GLP-1 RA users and nonusers, with procedures performed under both monitored anesthesia care and general anesthesia [69]. In parallel, multisociety clinical practice guidance describes that, in patients receiving GLP-1 RAs with concern for delayed gastric emptying or retained gastric contents, anesthetic technique selection may include consideration of general anesthesia with a secured airway, including rapid sequence induction and tracheal intubation, to minimize aspiration risk [70]. Overall, these data describe the use of both monitored anesthesia care and general anesthesia in patients receiving GLP-1 RAs, with general anesthesia providing a secured airway in situations where delayed gastric emptying or retained gastric contents are a concern. Non-operating room anesthesia safety has been evaluated largely in endoscopy-based cohorts, where sedation is commonly used, and concerns relate to retained gastric contents, aborted procedures, and aspiration-related complications. As described above, GLP-1 RA use has been associated with more frequent endoscopy discontinuation without an increase in pulmonary aspiration [58]. Additional observational studies have focused on surrogate procedural outcomes related to gastric contents. A matched case-control study of patients undergoing esophagogastroduodenoscopy reported higher rates of retained gastric contents and aborted procedures in GLP-1 RA users, while no anesthesia-related adverse events were observed [71]. Similarly, a retrospective case-control study of consecutive endoscopic procedures reported increased rates of solid gastric residue in patients taking GLP-1 RAs, particularly among those with type 2 diabetes and diabetic complications. In this cohort, some patients with retained contents required intubation or early procedure termination, while no procedural complications or aspiration events were recorded [72]. In a larger retrospective cohort of upper endoscopic procedures, GLP-1 RA use was associated with increased rates of procedure abortion due to retained gastric food, while no episodes of aspiration were observed among patients with retained contents [73]. Given this variability in retained gastric contents across individual studies, Table 1 synthesizes preoperative RGC findings across prospective cohorts, comparative studies, and pooled meta-analyses, stratified by GLP-1 RA agent and treatment indication.

Table 1: Preoperative RGC in patients receiving GLP-1 RAs, stratified by agent and treatment indication.

Agent	Dose/ Indication	Method	Gastric content: users vs. nonusers	Effect size; Reference
Semaglutide (SC weekly)	Weight-loss + glycemic mix, ≤10 days held[a]	Gastric ultrasound (prospective cohort)	40% (43/107) vs. 3% (3/113)	OR 36.97 (16.54–99.32) — Nersessian 2024 [35].
Semaglutide	Mixed, ≤7 days held (mostly ≤5)	Gastric ultrasound (prospective cross-sectional)	56% (35/62) vs. 19% (12/62)	~30.5% adj. absolute ↑ — Sen 2024 [1].
Semaglutide	Weight-loss + glycemic	EGD (retrospective cohort)	12.5% vs. 1.3%	Weight-loss 23% vs. diabetes 2.6% — Gu 2025 (n=1,045) [39].
Semaglutide vs. Tirzepatide	>6 mo use	EGD (retrospective)	11 of 12 chronic users had RGC (7 semaglutide / 4 tirzepatide)	Agent type not a significant predictor (p=NS) — Wen 2025 [30].
Semaglutide	Recently started, non-obese	Gastric ultrasound (prospective volunteer study)	Solids present after 8-h fast vs. controls	Volunteer study — Sherwin 2023 [31].
Semaglutide	Held 12 days, fasted 32 h	EGD (pediatric case report)	>200 mL confirmed content	Case report, held longer than ASA recommendation; gastric contents still present — Lookabaugh 2025 [74].

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Liraglutide / dulaglutide / exenatide	Mixed	EGD (network MA)[c]	No significant difference vs. semaglutide	χ^2=0.966, p=0.96 — Abdulraheem 2025 [75].
Mixed GLP-1 RAs (class)	Mixed	EGD, 13 studies (84,065 pts)	Pooled OR 5.56 (3.35–9.23)	Adj. OR 4.20[b]; diabetes subgroup OR 2.60 — Facciorusso 2025 [76].
Mixed GLP-1 RAs (class)	Mixed	EGD, 20 studies (207,708 pts)	Pooled OR 5.57 (4.07–7.62)	Adj. OR 3.18 — Abdulraheem 2025 [75].

[a] "Held" denotes the interval the agent was withheld before the procedure. [b] Adjusted odds ratios account for age, sex, body mass index, and diabetes status. [c] Network meta-analysis comparing semaglutide (oral and subcutaneous), exenatide, liraglutide, and dulaglutide. Abbreviations: adj., adjusted; CI, confidence interval; EGD, esophagogastroduodenoscopy; MA, meta-analysis; NS, not statistically significant; OR, odds ratio; RGC, residual gastric content; SC, subcutaneous; χ^2, chi-square; pts, patients.

Studies are ordered from prospective single-agent cohorts through direct head-to-head and network comparisons to pooled class-level meta-analyses. RGC was defined as any solid content or clear fluid volume >1.5 mL/kg on point-of-care gastric ultrasonography, or as retained gastric content directly visualized at endoscopy. Values are presented as prevalence (n/N) in exposed versus unexposed groups where reported; effect sizes are expressed as odds ratios with 95% confidence intervals. Methodological heterogeneity across studies of ultrasonography versus endoscopy, differing drug-withholding and fasting protocols, and mixed weight-loss and glycemic populations limits direct cross-study comparison. Increased RGC is a surrogate marker of aspiration risk and does not by itself denote clinically significant pulmonary aspiration. Interpretation of these findings is limited by the design of the underlying studies. Most data derive from retrospective endoscopy cohorts, which are susceptible to selection bias, as patients referred for endoscopy often have gastrointestinal symptoms or diabetic complications that independently slow gastric emptying [65,72]. Ascertainment bias is also possible, as retained contents may be documented inconsistently in procedural records. Confounding by indication is likely, given that GLP-1 RA users differ from nonusers in diabetes prevalence, body mass index, and concomitant medications. Prospective ultrasound studies reduce some of these biases but are smaller and often enroll selected populations. Differences in drug, dose, treatment phase, timing of the last dose, fasting protocols, and the definition used to identify RGC further limit cross-study comparison. Beyond these methodological differences, the wide range of effect sizes in Table 1 raises the question of whether clinical factors also contribute, particularly given that individual agents did not differ significantly in their association with RGC. One hypothesis is that dosing intensity contributes, since GLP-1 RAs are prescribed at higher, up-titrated doses for weight management than for glycemic control. However, since the primary studies did not report gastric content by administered dose, Table 2 compares findings by treatment indication. These comparisons cannot establish a dose-response relationship, as patients treated for weight loss and for diabetes also differ in body mass index, comorbidities, and treatment phase. Weight-loss regimens generally use higher doses than glycemic-control regimens, but these populations also differ in body mass index, comorbidities, and treatment phase; differences should not be interpreted as a dose-response relationship. Values represent RGC prevalence; odds ratios are shown where reported.

Together, Table 1 and Table 2 suggest that increased RGC is observed across GLP-1 RA agents, may be more prevalent among patients treated for weight loss, and is not reliably eliminated by prolonged withholding or extended fasting, although these observational comparisons cannot establish a dose-response relationship. This pattern supports individualized, risk-stratified perioperative management rather than fixed discontinuation timelines applied uniformly

Table 2: Preoperative RGC stratified by treatment indication and withholding interval.

Indication/Factor	Context	Residual gastric content (RGC)	Reference
Weight loss	Higher, up-titrated doses	~23%	Gu 2025 [39]
Glycemic control	Lower doses	~2.6% (Gu); diabetes subgroup OR 2.60 vs. nonusers (Facciorusso)	Gu 2025 / Facciorusso 2025 [39,76]
Withholding and fasting duration	≤7.5 days held + ≤21.3 h solid fast	Predicted high RGC	Pai 2026 [23]

[a] The "withholding and fasting duration" row reflects ultrasonography-derived thresholds: drug withholding of ≤7.5 days combined with a solid-food fast of ≤21.3 h predicted high RGC, suggesting that withholding duration and fasting duration should be considered together rather than relying on either alone. Abbreviations: OR, odds ratio; RGC, residual gastric content.

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across patients. Direct assessment tools, such as point-of-care gastric ultrasound, may complement consideration of withholding duration and fasting time, although their effect on aspiration outcomes has not been established.

Emergency Surgery and Full-Stomach Management

Emergency surgery represents a clinical context in which aspiration risk is influenced by uncertain fasting status and a higher prevalence of RGC at the time of induction. A prospective observational cohort study of 2,003 adults undergoing elective or emergency surgery found that high-risk gastric contents on preoperative ultrasound were more common in emergency procedures, with 21% of emergency patients classified as high risk compared with 14% of elective patients [77]. A large retrospective observational study of 166,491 anesthesia records reported that emergency procedures were associated with significantly increased risks of pulmonary aspiration and regurgitation without aspiration compared with elective procedures [64]. In pediatric populations, prospective observational data in children undergoing emergency appendectomy demonstrated that 32% had gastric contents considered higher risk for pulmonary aspiration, including solid or thick liquid contents [78]. These findings demonstrate substantial variability in gastric contents in emergency settings and highlight the limitations of relying on standard fasting intervals to predict gastric emptying. The persistence of higher-risk gastric contents across both adult and pediatric emergency patients supports an individualized approach to perioperative risk assessment at the time of induction, based on clinical context, procedural urgency, and patient-specific factors. This approach may help guide airway management and aspiration prevention strategies in higher-risk individuals.

Rapid Sequence Induction Guidelines and Practice Standards

Rapid sequence induction and other airway protection strategies are incorporated into anesthesia practice to reduce aspiration risk in patients with suspected full stomach physiology or uncertain gastric emptying. A 2023 update to preoperative fasting guidance addressed aspiration risk through standardized fasting durations and perioperative management of oral intake [79]. More recent GLP-1 RA-specific guidance has incorporated these medications into existing aspiration risk frameworks. Clinical practice recommendations from Australia and New Zealand advise screening for GLP-1 RA use prior to anesthesia or sedation and recommend a 24-hour clear fluid diet followed by standard fasting, with gastric ultrasound or minimally sedated gastroscopy as additional options for risk stratification when fasting adequacy is uncertain [80]. These guidelines further state that patients who do not undergo risk mitigation strategies should be considered to have a full stomach and be managed with appropriate aspiration precautions, including consideration of rapid sequence induction [71,80]. Similarly, a multidisciplinary consensus statement from UK perioperative organizations recommends that patients taking GLP-1 RAs undergo individualized risk assessment and receive perioperative techniques to mitigate pulmonary aspiration risk before, during, and after anesthesia, including airway management strategies such as modified rapid sequence induction [81]. During anesthetic management, these recommendations situate GLP-1 RA use within established full stomach precautions, where airway management strategies such as rapid sequence induction are considered alongside other clinical indicators of delayed gastric emptying and aspiration risk.

Evolution of Perioperative Guidelines and Consensus Statements

Early perioperative guidance regarding GLP-1 RAs emerged in response to rapidly evolving evidence suggesting potential aspiration risk despite adherence to standard fasting protocols [57]. In less than one-year, multiple case reports and observational studies reported the presence of significant RGC in patients receiving GLP-1 RAs, prompting reconsideration of their perioperative safety [26,31,33,34,55,56]. Historically, these medications were continued perioperatively without modification to anesthetic technique, as earlier data suggested delayed gastric emptying had minimal clinical impact and was not associated with major safety concerns. Subsequent observational evidence also demonstrated a higher incidence of RGC in fasting patients receiving these agents, including one cohort study reporting an adjusted odds ratio of 5.8 for visible gastric contents [57]. These findings contributed to a shift in clinical concern from a previously theoretical risk to a clinically relevant perioperative issue, reinforcing early precautionary recommendations by anesthesia societies and expert groups. Editorial and correspondence literature emphasized that accumulating evidence supported the plausibility that delayed gastric emptying may translate into increased aspiration risk, leading to reconsideration of standard fasting practices [82]. In 2023, the ASA Task Force on Preoperative Fasting released consensus-based guidance recommending preoperative withholding of GLP-1 RAs and treating patients who had not withheld therapy as having a “full stomach” [18,57]. Concurrent editorial guidance similarly advocated for the preoperative discontinuation of GLP-1 RAs, although recommended withholding durations varied substantially, reflecting uncertainty in the existing evidence base. Despite these precautionary approaches, early guidance was characterized by significant uncertainty and heterogeneity. Editorial discussions highlighted that recommended withholding intervals were largely based on limited and indirect evidence, and that key questions regarding optimal timing, duration of effect, and true aspiration risk remained unresolved [83]. This uncertainty was further highlighted by ongoing debates regarding mechanisms such

as tachyphylaxis and the duration-dependent effects of GLP-1 RAs on gastric emptying. At the same time, the literature noted a lack of clinical evidence supporting different perioperative management strategies based on the duration of drug use. Collectively, early perioperative guidance was driven by emerging safety signals rather than definitive evidence, resulting in conservative recommendations, variability across sources, and recognition of substantial knowledge gaps [82].

Multisociety Guidance and Risk-Based Perioperative Management

Updated perioperative guidance has evolved with the publication of a 2024 multisociety guidance document that provides recommendations for the management of patients receiving GLP-1 RA therapy [60]. The objective of this guidance was to offer unified recommendations for clinicians while recognizing inconsistencies across existing clinical guidelines between associations and the resulting uncertainty in how to safely manage these patients. These recommendations emphasize shared decision making between the anesthesia provider, prescribing clinician, and patient when determining perioperative medication management. However, accompanying editorial discussions highlight that differences persist between organizations regarding how GLP-1 RAs should be managed in the perioperative period, and that clinical guidelines remain variable with ongoing uncertainty [84,85]. Accompanying editorials and commentary have emphasized that updated perioperative recommendations remain contested and are based on limited evidence. One editorial stated that there are differences between regulatory agencies and organizations in how GLP-1 RAs should be managed in the perioperative period and argued that these medications should continue during the perioperative period [84]. The same commentary noted that the evidence supporting the ASA recommendations was essentially limited to a single case report and two retrospective case studies and further stated that no other organization or regulatory body had replicated these recommendations. In that context, the authors concluded that, in the absence of conclusive data supporting updated ASA guidance, GLP-1 RAs may be continued with individualized risk assessment and appropriate precautions. A separate editorial also noted conflicting recommendations, a lack of good-quality evidence on the perioperative use of GLP-1 RAs and observed that differences in major clinical guidelines create challenges for decision-making in patient care [85]. From a clinical perspective, updated multisociety guidance recommends adjusting perioperative management for patients receiving GLP-1 RAs based on each patient's individual risk. Patient-specific factors should be considered when assessing the risk of delayed gastric emptying and pulmonary aspiration, as risk may be higher in patients in the escalation phase, on higher doses, or receiving weekly dosing [70]. In lower-risk patients, continuation of GLP-1 RAs may be appropriate, whereas in higher risk patients, decisions regarding withholding therapy should balance surgical and metabolic risks. Conservatively withholding GLP-1 RAs also carries risks. In patients with diabetes, stopping therapy may cause perioperative hyperglycemia [70]. Additionally, for those taking these agents for weight management or cardiovascular risk reduction, withholding may interrupt treatment of conditions for which GLP-1 RAs provide an established long-term benefit [6,9]. Current guidance therefore supports continuing therapy in most patients, especially those without risk factors for delayed gastric emptying, while weighing aspiration risk against the consequences of interrupting therapy [70,81]. If therapy is withheld, the decision should be coordinated with the prescribing clinician, with perioperative glucose monitoring and a plan to restart treatment after the procedure [70].

Evolving and Divergent Perioperative Recommendations for GLP-1 Receptor Agonists

Emerging evidence from perioperative and endoscopic contexts has raised concern regarding the presence of retained gastric contents and potential aspiration risk in patients receiving GLP-1 RAs. Case reports have described pulmonary aspiration despite "adequate" fasting, including instances of regurgitation of large volumes of gastric contents following prolonged preoperative fasting [86]. Observational data further support these findings, with studies demonstrating a significantly increased risk of RGC in patients receiving GLP-1 RAs compared with controls, and evidence that gastric contents may persist despite appropriate fasting and even prolonged discontinuation of therapy [83]. Data from endoscopy-based studies further characterize the relationship between GLP-1 RA use, retained gastric contents, and clinical outcomes. Patients receiving GLP-1 RAs have been reported to have higher rates of RGC compared with controls, even when fasting durations exceeded recommended intervals [87]. However, the relationship between retained gastric contents and clinically observed aspiration events remains less clear. In the cohorts, pulmonary aspiration events have been infrequently reported, with rates comparable to those expected in endoscopic procedures [87]. Divergence in specialty-specific recommendations has emerged because of ongoing uncertainty in the available evidence. The ASA's 2023 consensus-based guidance recommended withholding GLP-1 RAs prior to procedures, whereas gastrointestinal societies advocated for an individualized approach to management in patients undergoing endoscopy [22,88]. The ASA subsequently participated in the 2024 multisociety guidance, which favors individualized, risk-stratified management [70]. Although U.S. recommendations have since converged on this approach, this earlier divergence reflected broader controversy surrounding perioperative continuation of these medications [84]. Differences in recommended precautions persist across international guidance, reflecting data on aspiration risk that remain limited and inconclusive

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[80,81,85]. Consistent with this, gastrointestinal society statements have emphasized that there is insufficient evidence to support routine discontinuation of GLP-1 RAs prior to elective endoscopic procedures [87]. Table 3 summarizes the chronology, scope, and key recommendations of major professional society guidance, illustrating the shift from routine withholding toward individualized, risk-stratified management.

Table 3: Chronology of perioperative GLP-1 RA guidance by professional societies.

Guidance (year)	Issuing bodies	Scope	Recommendation on GLP-1 RA therapy	Additional precautions
ASA (2023) [22]	American Society of Anesthesiologists	Elective procedures; adults and children	Hold daily agents on day of procedure; hold weekly agents 1 week prior	GI symptoms: consider delay. Not held: full-stomach precautions or gastric ultrasound
AGA (2023) [88]	American Gastroenterological Association	Endoscopy	Routine withholding not supported; individualized approach	Liquid diet the day before as an alternative; RSI if symptomatic and delay is undesirable
Multisociety (2024) [70]	ASMBS, ASA, AGA, ISPCOP, SAGES	Elective surgery and endoscopy	Continuation in most patients; shared decision-making	Higher-risk patients: 24-h liquid diet and adjusted anesthetic plan
UK (2025) [81]	Association of Anaesthetists, RCoA, and six other UK bodies	Elective surgery and sedation; includes GIP/GLP-1 agonists	Continue before surgery	Full risk assessment; gastric ultrasound, regional anesthesia, airway precautions
Australia/NZ (2025) [80]	ADS, ANZCA, GESA, NACOS	Surgery and endoscopy; includes GIP/GLP-1 agonists	Diet modification for all patients	24-h clear fluid diet, then 6-h fast; gastric ultrasound or full-stomach precautions if not completed

All recommendations are based on expert consensus rather than high-quality comparative evidence. Recommendations are summarized for elective procedures. The ASA subsequently affirmed the 2024 multisociety guidance. Abbreviations: ADS, Australian Diabetes Society; AGA, American Gastroenterological Association; ANZCA, Australian and New Zealand College of Anaesthetists; ASA, American Society of Anesthesiologists; ASMBS, American Society for Metabolic and Bariatric Surgery; GESA, Gastroenterological Society of Australia; GI, gastrointestinal; ISPCOP, International Society of Perioperative Care of Patients with Obesity; NACOS, National Association of Clinical Obesity Services; RCoA, Royal College of Anaesthetists; RSI, rapid sequence induction; SAGES, Society of American Gastrointestinal and Endoscopic Surgeons.

Future Directions

The perioperative management of patients receiving GLP-1 RAs remains an evolving area of investigation, with several unresolved questions limiting the development of evidence-based recommendations. Existing studies have primarily focused on physiologic and surrogate measures, such as gastric emptying and RGC, while their relationship to clinically meaningful aspiration events has not been clearly established. Prospective observational data have emphasized that the presence of RGC does not directly establish aspiration risk, and future studies should evaluate clinical outcomes such as aspiration events and pulmonary complications in patients receiving GLP-1 RAs. Uncertainty also persists regarding optimal perioperative management strategies, particularly with respect to medication withholding. Although delayed gastric emptying has been frequently observed with GLP-1 RAs, it remains unclear whether this translates into increased perioperative aspiration risk, and the optimal duration of discontinuation prior to surgery is not well defined. These limitations are further compounded by heterogeneity across agents, dosing regimens, and treatment duration, as well as the increasing use of combination therapies, which limit the generalizability of existing findings across the drug class. The temporal variability of GLP-1 RA effects represents an additional area of uncertainty. Available data suggest that delayed gastric emptying may attenuate with continued GLP-1 RA therapy, although the consistency of this effect and its relevance to perioperative risk remain unclear. Longitudinal studies evaluating both gastric physiology and perioperative outcomes across different phases of treatment may help clarify whether risk differs between early treatment and stable long-term use. Similarly, while preoperative gastric ultrasound has been proposed as a tool for individualized risk assessment, its role in guiding perioperative management decisions in this population has not been prospectively validated. Finally, the broader clinical implications of perioperative GLP-1 RA management extend beyond aspiration risk alone. The effects of continuation or discontinuation on glycemic control, cardiovascular stability, and perioperative metabolic outcomes have not been systematically evaluated. A comprehensive perioperative framework will require integration of both anesthetic and metabolic considerations to better define risk-benefit tradeoffs and inform future clinical guidance.

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Limitations

The available evidence examining the perioperative implications of GLP-1 RA use should be interpreted in the context of several limitations. To date, no randomized controlled trials have evaluated pulmonary aspiration as a primary outcome in patients receiving GLP-1 RAs undergoing anesthesia. Existing evidence is derived predominantly from observational cohort studies, case series, and case reports, which are inherently subject to confounding and do not permit causal inference. Interpretation is further limited by the low incidence of pulmonary aspiration, as even large retrospective cohorts remain underpowered to detect meaningful differences in event rates between exposed and unexposed groups. In addition, most perioperative investigations rely on surrogate markers such as gastric volume or the presence of RGC as indicators of aspiration risk. While these measures reflect underlying physiologic effects, they have not been prospectively validated against clinically confirmed aspiration outcomes in this population. Notably, although retained gastric contents are generally observed more frequently among GLP-1 RA users, this has not been associated with a corresponding increase in aspiration events, and the clinical significance of this discrepancy remains uncertain. The literature is also characterized by substantial heterogeneity in study design and exposure definitions, including variation in GLP-1 RA agents, dosing regimens, duration of therapy, and timing of the last administered dose. Short-acting and long-acting formulations have distinct pharmacokinetic profiles and may differ in their effects on gastric motility. However, many studies evaluate these agents collectively or focus on a single formulation, limiting generalizability across the drug class. Finally, confounding by indication remains a persistent limitation. Patients receiving GLP-1 RAs are more likely to have comorbid conditions such as type 2 diabetes and obesity, both of which independently influence gastric emptying and aspiration risk. Although some studies adjust for these variables or use active comparator designs, residual confounding cannot be excluded, making it difficult to isolate the independent contribution of GLP-1 RA therapy. Furthermore, the potential contribution of concomitant medications known to slow gastric emptying was not consistently accounted for across the literature, which may have amplified the observed association between GLP-1 RA use and retained gastric contents in some studies. In addition, much of the available evidence is derived from endoscopy-based and non-operating room anesthesia settings, which may not fully reflect risk in broader surgical populations. This review is also subject to methodological constraints: as a narrative review without formal risk-of-bias assessment, study selection and synthesis may reflect author judgment, and restriction to English-language studies in two databases may have omitted relevant evidence. These limitations highlight the need for cautious interpretation of the current evidence and emphasize the evolving nature of this field.

Conclusion

The perioperative implications of GLP-1 RA therapy reflect a complex interaction between well-characterized physiologic effects on gastric motility and inconsistently observed clinical outcomes during anesthesia. Across mechanistic and perioperative studies, GLP-1 RAs are frequently linked to delayed gastric emptying and an increased prevalence of RGC despite adherence to standard fasting guidelines. These findings have raised concern for aspiration risk and have prompted changes in perioperative management strategies, including modifications to fasting recommendations and airway management approaches. However, the current clinical evidence does not demonstrate a clear increase in pulmonary aspiration or aspiration-related complications among patients receiving GLP-1 RAs. Observational cohort studies across endoscopic and perioperative settings generally report low rates of aspiration events, even in the presence of retained gastric contents. This discrepancy between physiologic markers and clinical outcomes underscores a central limitation in the existing evidence, suggesting that RGC alone may not reliably predict aspiration risk in this population. Within this context, perioperative risk appears to be multifactorial and influenced by patient characteristics, procedural factors, and anesthetic technique rather than GLP-1 RA use in isolation. The variability observed across studies, including differences in drug exposure, timing of administration, and patient comorbidities, further supports an individualized approach to perioperative management. Current guidance increasingly reflects this perspective, emphasizing risk stratification and clinical context rather than uniform discontinuation strategies. Despite the rapid expansion of the literature, substantial uncertainty remains regarding optimal perioperative management. In particular, it is unclear whether current precautionary approaches meaningfully reduce aspiration risk or whether they introduce unintended consequences related to medication interruption. Further prospective studies evaluating clinically relevant outcomes will be necessary to clarify the relationship between delayed gastric emptying and aspiration risk and to inform evidence-based perioperative guidelines for patients receiving GLP-1 RAs.

Key Points

- GLP-1 receptor agonists (GLP-1 RAs) delay gastric emptying through combined central (vagally mediated) and peripheral (enteric) mechanisms, an effect that has been consistently demonstrated across multiple study designs.
- Despite adherence to the standard American Society of Anesthesiologists fasting guidelines, GLP-1 RA users consistently show a higher prevalence of residual gastric content (RGC) than nonusers across multiple prospective and retrospective cohorts, regardless of detection method or specific agent studied.

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- Preoperative withholding duration and overall treatment duration both appear to have limited value in predicting reduced gastric content, as recent or higher-intensity dosing can still carry an elevated risk regardless of either timeline.
- Multiple measures of gastric emptying and content, including gastric ultrasound, scintigraphy, acetaminophen absorption testing, and endoscopy, are increasingly used to support individualized perioperative risk assessment, offering a more direct evaluation than reliance on fasting duration alone.
- Despite the consistent association between GLP-1 RA use and increased RGC, large observational cohorts have not demonstrated a corresponding increase in pulmonary aspiration or aspiration-related complications in the perioperative setting, revealing a discrepancy that limits firm conclusions about the true risk posed by GLP-1 RA use during anesthesia or sedation.
- Aspiration risk in patients receiving GLP-1 RAs appears multifactorial, influenced by procedural urgency, concurrent medications, airway characteristics, and patient comorbidities rather than GLP-1 RA use in isolation.
- The magnitude of RGC risk appears to scale with dosing intensity rather than being specific to any single agent, with higher-dose regimens for weight loss being associated with greater retained gastric content than lower-dose regimens for glycemic control.
- Professional society guidance on the perioperative management of GLP-1 RA therapy remains divergent, with some organizations favoring preoperative discontinuation and full-stomach precautions while others caution that discontinuation may forfeit glycemic and metabolic benefits without clear evidence of improved safety, reflecting uncertainty and limited evidence in the field.
- Given the absence of randomized controlled trials with aspiration as a primary outcome, perioperative management of GLP-1 RA therapy should favor individualized, risk-stratified decision-making over uniform discontinuation policies.

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