# Perioperative Management of Patients Taking Glucagon-like Peptide-1 Receptor Agonists: Applying Evidence to Clinical Practice

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Glucagon-like peptide-1 (GLP-1) receptor agonists, introduced in clinical practice in 2005, have revolutionized the treatment of type 2 diabetes, and their use represents a paradigm shift. GLP-1 receptor agonists have allowed for better control of glycemia when compared to basal insulin with minimal risk of hypoglycemia.[1] The number of prescriptions for this medication class have risen sharply, with introduction of new pharmacologic agents and the wide adoption of GLP-1 receptor agonists for treatment of obesity. Clinicians frequently care for patients prescribed GLP-1 receptor agonists and need to be familiar with perioperative considerations. The anesthetic plan needs to be tailored based on the specific drug, the dosing schedule, fasting time, gastrointestinal symptoms, and the planned procedures. In this article, we discuss the pharmacokinetics of GLP-1 receptor agonists, mitigating factors affecting risks of aspiration, and risks and benefits of stopping or continuing GLP-1 receptor agonists perioperatively. We also propose a framework for periprocedural management of patients taking GLP-1 receptor agonists.

## Perioperative Concerns and Currently Recommended Management

The clinical benefits of GLP-1 receptor agonists are derived partly through their propensity to slow down gastrointestinal motility. In the outpatient setting, reported gastrointestinal adverse events related to GLP-1 receptor agonists have risen as their utilization has surged.[2] Most commonly reported side effects are abdominal pain (57.6%), nausea and vomiting (23.4%), constipation (30.4%), and diarrhea (32.7%).[3] Gastrointestinal side effects occur for both short- and long-acting preparations, and for subcutaneously and orally administered preparations. Typically, these adverse effects are not serious, are self-limited, and are more pronounced at the initiation of the drug or during dose escalation phases. They often subside when maintenance doses are reached.

GLP-1 receptor agonists' ability to slow gastric emptying to a gastroparesis level has translated into concerns for perioperative aspiration.[4,5] Multiple case reports, case series, and studies have been published since 2022.[6–21] These concerns led the American Society of Anesthesiologists (ASA; Schaumburg, Illinois) to publish a consensus-based guidance suggesting that patients discontinue GLP-1 receptor agonists for 1 day for short-acting preparations and 1 week for long-acting preparations, while observing the current ASA fasting guidelines without any modifications.[22] However, the ASA recommendations have been questioned because of the lack of data supporting them and new data that are rapidly emerging.

## GLP-1 Receptor Agonists and Their Pharmacologic Properties

There are several GLP-1 receptor agonists currently available (table 1). Short-acting preparations include lixisenatide and exenatide. The lixisenatide-alone formulation was withdrawn from the United States market in January 2023 but remains available in Europe. Lixisenatide is currently available only in combination with long-acting insulin in the United States. Exenatide is available as a short-acting twice-daily subcutaneous preparation or as a long-acting weekly formulation with the drug slowly released from a matrix. Other long-acting GLP-1 receptor agonists include liraglutide, dulaglutide, and semaglutide. Liraglutide is mostly albumin-bound, thus having a reservoir for prolonged release, which accounts for its long half-life.[26] Dulaglutide is a GLP-1 molecule coupled with an immunoglobulin Fc fragment leading to slow degradation. Semaglutide is available in two forms: a weekly long-acting preparation, which is albumin-bound, and an oral form with low bioavailability after ingestion leading to the need for daily dosing.[26]

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**Table 1.** GLP-1 Receptor Agonist Medications, Their Pharmacologic Properties, and Indications

| Medication (Brand Name) | Administration | Half-life | Time to Peak Effect | Steady State | Dose Escalation | Indication |
|---|---|---|---|---|---|---|
| **Short-acting GLP-1 receptor agonist** | | | | | | |
| Exenatide (Byetta; AstraZeneca, UK) | Subcutaneous twice daily | 3.3–4 h | 3 h | | 5 μg for 1 mo,<br>10 μg (maximum dose) | Diabetes |
| Lixisenatide (Lyxumia; Sanofi, France) | Subcutaneous once daily | 2.6 h | 2 h | | 10 μg for 2 wk, 20 μg (maximum dose) | Diabetes |
| **Long-acting GLP-1 receptor agonist** | | | | | | |
| Exenatide (Bydureon BCise; AstraZeneca) | Subcutaneous once weekly | | 4–8 h | 6–7 wk[23] | 2 mg weekly | Diabetes |
| Liraglutide (Victoza, Saxenda; Novo Nordisk, Denmark) | Subcutaneous once daily | 12.6–14.3 h | 12 h | 3 d[24] | 0.6 mg for 1 wk,<br>1.2 mg for 1 wk,<br>1.8 mg (maximum dose) | Diabetes (Victoza)<br>Obesity (Saxenda) |
| Dulaglutide (Trulicity; Eli Lilly, USA) | Subcutaneous once weekly | 4.7–5.5 d | 48 h | 2–4 wk[25] | 0.75 mg for 4 wk,<br>1.5 mg for 4 wk,<br>4.5 mg (maximum dose) | Diabetes |
| Semaglutide (Ozempic, Wegovy; Novo Nordisk) | Subcutaneous once weekly | 5.7–6.7 d | 24 h | 4–5 wk | 0.25 mg for 4 wk,<br>0.5 mg for 4 wk,<br>1 mg for 4 wk,<br>1.7 mg for 4 wk (Wegovy)<br>2.4 mg (Wegovy maximum dose); 2 mg (Ozempic maximum dose)<br>3 mg for 4 wk,<br>7 mg for 4 wk,<br>14 mg (maximum dose) | Diabetes (Ozempic)<br>Obesity (Wegovy, Rybelsus) |
| Semaglutide (Rybelsus; Novo Nordisk) | Oral once daily | 5.7–6.7 d | 1–4 h | | | |
| **Dual GLP-1/GIP receptor agonist** | | | | | | |
| Tirzepatide (Mounjaro, Zepbound; Eli Lilly) | Subcutaneous once weekly | | 8–72 h | 4 wk | 2.5 mg for 4 wk, escalate by 2.5 mg every 4 wk up to 15 mg (maximum dose) | Diabetes (Mounjaro)<br>Obesity (Zepbound) |

GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1.

Tirzepatide is a dual GLP-1 receptor agonist and glucose-dependent insulinotropic polypeptide (GIP) dosed weekly and approved for treatment of diabetes mellitus and obesity. The various GLP-1 receptor agonists and their pharmacologic properties are presented in table 1. Orforglipron, a daily oral GLP-1 receptor agonist, and retatrutide, a triple GLP-1, GIP, and glucagon receptor agonist administered subcutaneously, are in late phases of development.[27–29]

## Perioperative Considerations

General principles guiding perioperative medication management include a thoughtful assessment of the risks and benefits of continuing or discontinuing a medication based on the indication, pharmacokinetics, and potential interactions with anesthetic agents. In certain circumstances, the planned procedure and the anesthetic are important considerations. Medications are withheld perioperatively in select circumstances when risks are perceived to outweigh benefits and no alternative measures can mitigate the periprocedural risks.

## Benefits *versus* Risks of Continuing GLP-1 Receptor Agonists

In patients with diabetes mellitus, GLP-1 receptor agonists reduce glycemia through multiple mechanisms such as slowing gastric emptying, increasing pancreatic insulin secretion, decreasing glucagon release, and decreasing appetite.[30,31] In the outpatient setting, cardiovascular outcome trials and metanalyses demonstrate that GLP-1 receptor agonists reduce major adverse cardiovascular events, including acute myocardial infarction, stroke, and mortality in individuals with multiple cardiovascular risk factors and either type 2 diabetes or obesity.[32–34] The American Diabetes Association (Arlington, Virginia) and the American Association of Clinical Endocrinology (Jacksonville, Florida) recommend GLP-1 receptor agonists as first-line drugs along with metformin for patients with type 2 diabetes with an established or high risk of atherosclerotic cardiovascular disease, stroke, transient ischemic attacks, or chronic kidney disease.[35,36]

There are emerging data of the *benefits* of continuing GLP-1 receptor agonists during the perioperative period specifically in patients with diabetes mellitus.

- Studies in cardiac surgery show glycemia benefit of GLP-1 receptor agonists (liraglutide and exenatide) when compared to insulin, and delayed initiation and lower doses of insulin needed for glycemic control[37–42] (table 2).
- Benefits of GLP-1 receptor agonist such as better glycemia control and fewer prosthetic joint infections have been described in patients having noncardiac surgeries. These effects are possibly explained by the

immunomodulatory and anti-inflammatory effects of GLP-1 receptor agonists[43,44] (table 2).
- There is a lack of data on the benefits of continuing GLP-1 receptor agonists in patients with obesity, because all the studies to date have been performed in patients with diabetes mellitus.

The perioperative *risks* of continuing GLP-1 receptor agonists pertain to their propensity to delay gastric emptying, and concerns for perioperative aspiration of gastric contents. Self-reported symptomatology such as nausea and vomiting suggests delayed gastric emptying.[45] However, lack of symptoms correlate poorly with gastric emptying. Data show that even when patients report no symptoms, they can still have significantly altered gastric emptying times.[45] Evidence of delayed gastric emptying from GLP-1 receptor agonist comes from case reports and case series (table 3) and from outpatient gastric emptying studies (table 4).[6–21,46–88]

A summary of studies and case reports of aspiration events and residual gastric contents assessed by ultrasonography or endoscopy is shown in table 3.

- It is notable that in these reports, the patients followed current recommendations for fasting (*i.e.*, 8 h fasting time for solids and 2 h for liquids).[89]
- Although the number of aspiration events is small, the vast majority occurred in patients receiving monitored anesthesia care. In a retrospective database review of patients having esophagogastroduodenoscopy, the only two aspiration events occurred in patients receiving monitored anesthesia care, and aspiration rates were comparable to those seen in the general population of patients receiving anesthesia.[19]
- The risk of aspiration does not appear to be increased in patients having emergency surgeries who have not had time to stop their GLP-1 receptor agonist, which may be partly due to the use of rapid sequence induction and intubation.[20] Also, general endotracheal anesthesia seems to protect against the risk of aspiration.[48]

While the risk of aspiration is present and should not be underappreciated, the evidence for delayed gastric emptying primarily comes from outpatient data. The data on gastric emptying in patients on GLP-1 receptor agonist are heterogeneous in nonprocedural and nonsurgical settings (table 4), and interpretation is nuanced.

- These data are mixed with respect to the method used to assess gastric emptying; the studied population, which included patients with obesity, diabetes, or healthy volunteers; the reported results; and perioperative relevance.
- The most accurate assessment of gastric emptying is the nuclear scintigraphic method, which evaluates solid food retention in the stomach. The gastric motility breath test is another infrequently used study to measure solid content transit times. However, few studies have assessed gastric emptying in patients taking GLP-1 receptor agonist using these methods. A recent metanalysis of studies looking at GLP-1 receptor agonist effects on gastric emptying reported prolonged times required for 50% of ingested gastric contents to leave the stomach. Patients taking GLP-1 receptor agonist had a time required for 50% of ingested gastric contents to leave the stomach of 138.4 min (95% CI, 74.5 to 202.3) *versus* 95.0 min (95% CI, 54.9 to 135.0) for the placebo group, with a pooled mean difference of 36.0 min ($P < 0.01$).[88] This evidence supports a delayed gastric emptying of solid foods being decreased in patients taking GLP-1 receptor agonists.
- The majority of studies have used an acetaminophen absorption test, which assesses gastric emptying of liquids rather than solids. Consequently, many experts consider data obtained from acetaminophen absorption studies inadequate to base clinical decisions ofor patients on GLP-1 receptor agonists.[88] A metanalysis of 10 studies with 411 individuals using an acetaminophen test showed no significant delay in gastric emptying at 1, 4, and 5 h in patients taking GLP-1 receptor agonist.[90] These data point toward normal emptying of liquids in these patients.
- There is a difference between short- and long-acting drugs and their effects on gastric emptying. The plasma concentration of short-acting drugs peaks and decreases rapidly. This intermittent stimulation of the GLP-1 receptor may impact gastric emptying more than occurs with long-acting drugs, which continuously stimulate receptors, resulting in tachyphylaxis. It may take weeks to months for patients on short-acting medications to develop tachyphylaxis compared to 4 to 5 weeks for long-acting preparations.[73]
- Data on tachyphylaxis for long-acting preparations are mixed as well, with some studies showing that even long-acting preparations (liraglutide, weekly semaglutide, long-acting exenatide) significantly delay gastric emptying.[62,65,67] These data are corroborated by a metanalysis reporting that the type of GLP-1 receptor agonist did not correlate with the gastric emptying effects regardless of the type of assessment (scintigraphy or acetaminophen absorption).[90]
- Gastric emptying studies have not assessed effects beyond 4 to 6 h. The limited evidence from emptying studies using scintigraphy have detected a prolongation (138 *vs.* 95 min) of gastric emptying measured at 4 h, which is much less than the recommended fasting time for solids, but longer than that recommended for liquids.
- Gastric emptying effects are more pronounced in the first few weeks after initiating GLP-1 receptor agonists or escalating doses. During this time, gastric emptying for liquids can be prolonged as assessed by acetaminophen tests.[13,87]

Overall, while the current gastric emptying studies may be difficult to interpret and extrapolate to the perioperative setting, the data point toward a prolonged

**Table 2.** Studies on Perioperative Benefit of GLP-1 Receptor Agonists

| Reference | Type of Study | GLP-1 Receptor Agonist | Study Protocol | Results |
|---|---|---|---|---|
| **Cardiac surgery** | | | | |
| Polderman[37] 2018 | Randomized controlled trial | Liraglutide | Liraglutide 0.6 mg subcutaneously the evening before procedures and 1.2 mg the day of the procedures *vs.* insulin by infusion or bolus. | • Mean plasma glucose concentrations 1 h postoperatively were significantly lower in the liraglutide group (6.6 mM) *vs.* the insulin infusion (7.5 mM; $P = 0.026$) and bolus groups (7.6 mM; $P = 0.006$)<br>• No difference in the incidence of hypoglycemia and postoperative complications between groups |
| Hulst[38] 2020 | Randomized controlled trial | Liraglutide | Liraglutide 0.6 mg subcutaneously the evening before procedures and 1.2 mg after anesthesia induction in patients with low nausea scores *vs.* insulin protocol. | • Mean blood glucose concentrations, and dose and number of insulin injections, were lower in liraglutide group *vs.* insulin protocol group<br>• No difference in the incidence of hypoglycemia, mortality, and postoperative complications between groups |
| Makino[39] 2019 | Randomized controlled trial | Liraglutide | Liraglutide 0.3 mg subcutaneously on days –2 and –1, and 0.6 postoperative days 1 to 10 in addition to insulin. | • Glucose concentrations closer to target range in the combination group *vs.* insulin-only group<br>• Lower incidence of hypoglycemia in the liraglutide group |
| Lipš[40] 2017 | Randomized controlled trial | Exenatide | Exenatide or placebo, continuous 72-h IV infusion plus standard perioperative insulin therapy starting 12 h before surgery. | • Improved perioperative glucose control with exenatide, with average glucose 6.4 mM (exenatide) *vs.* 7.3 mM (placebo); $P < 0.001$)<br>• Glucose concentration in the target range of 4.5 to 6.5 mM in the exenatide group 54.8% of the time *vs.* 38.6% in the control group ($P = 0.001$)<br>• No difference in hypoglycemia risk between groups |
| Besch[41] 2017 | Randomized controlled trial | Exenatide | Exenatide infusion. | • Exenatide failed to show superior glycemia values in patients having coronary artery bypass grafting, but exenatide reduced overall consumption of and delayed time to initiation of insulin compared to controls |
| **Noncardiac surgery** | | | | |
| Kaneko[43] 2018 | Randomized controlled trial | Liraglutide | Liraglutide 0.6 mg subcutaneously at least a week before procedures; dose doubled every 1 to 2 days if no reported gastrointestinal symptoms. Liraglutide reduced by 0.6 mg on the day of surgery and postoperative day 1, and then increased to the previous maximum on postoperative day 2. | • More stable glucose concentrations with liraglutide, fewer patients requiring additional insulin ($P = 0.005$), and a significant reduction of the insulin dosage on day of surgery ($P = 0.004$) in patients having orthopedic, thoracic, otolaryngological, urological, hepatic, gynecological, and breast surgeries |
| Magruder[44] 2024 | Observational | Semaglutide | Semaglutide *vs.* no GLP-1 receptor agonist. | • In patients with diabetes mellitus having primary hip arthroplasties, semaglutide had lower rates of readmissions within 90 days of surgery (6.2% *vs.* 8.8%; $P < 0.01$) and fewer prosthetic joint infections (1.6 *vs.* 2.9%; odds ratio, 0.56; $P < 0.01$) compared to patients with diabetes mellitus not on a GLP-1 receptor agonist |

GLP-1, glucagon-like peptide-1; IV, intravenous.

gastric emptying time for solids. In addition, the presence of residual gastric contents directly observed *via* endoscopy in patients fasting for solids between 8 and 18 h provides irrefutable evidence that gastric emptying time for solids is affected, regardless of the duration of therapy or patients being in a maintenance phase.[12,21] While effects on gastric emptying for solids are more pronounced with short-acting preparations and long-acting GLP-1 receptor agonists during therapy initiation or dose escalation, some studies show delays in gastric emptying even during the maintenance phase. Emptying time for liquids may not be as significantly impacted with long-acting preparations during steady state due to tachyphylaxis. However, liquid emptying remains slightly prolonged with short-acting preparations, and during start of therapy or dose escalation periods with long-acting GLP-1 receptor agonists.[13,86]

## Benefit *versus* Risks of Stopping GLP-1 Receptor Agonists

The potential *benefit* of stopping GLP-1 receptor agonists for only one pharmacologic half-life has come under scrutiny. There are several considerations that counter the benefit of stopping the GLP-1 receptor agonist, including the following:

- Pharmacokinetic data demonstrate that there is residual circulating drug after missing one dose of both short- and long-acting GLP-1 receptor agonists.
  - Pharmacokinetic modeling of liraglutide shows that at the end of one half-life of elimination, the blood concentration is higher in patients taking 1.8 mg compared to the peak concentration of liraglutide 0.6 mg[24] (fig. 1).
  - The simulated semaglutide concentration dosed at 1 mg showed that when missing one dose, there was

**Table 3.** Clinical Evidence of Decreased Gastric Emptying in Patients Taking GLP-1 Receptor Agonists

| Author | GLP-1 Receptor Agonist (No. of Patients) | Study Type | Indication for GLP-1 Receptor Agonist | Procedure/ Anesthetic | Length of Fasting | Findings | Comments |
|---|---|---|---|---|---|---|---|
| **Aspiration events or regurgitation of gastric contents** | | | | | | | |
| Gulak and Murphy[6] | Semaglutide | Case report | Obesity | Breast lumpectomy with general anesthesia | 20 h (solids), 8 h (liquids) | Regurgitation of gastric contents upon standard induction | Semaglutide 0.5 mg for 5 mo, taken 2 days before surgery |
| Klein and Hobai[7] | Semaglutide | Case report | Obesity | Upper endoscopy with monitored anesthesia care | 18 h | Increased residual gastric contents before endotracheal intubation | Semaglutide started 2 mo before procedure, most recent dose 1.7 mg |
| Avraham *et al.*[9] | Semaglutide (n = 2) | Case report | Obesity, type 2 diabetes | General anesthesia for endoscopic retrograde cholangiopancreatography and breast abscess | 8–12 h | Regurgitation of gastric contents | Semaglutide 1 mg taken 4 and 6 days before procedure |
| Weber *et al.*[46] | Tirzepatide | Case report | Obesity | General anesthesia with supraglottic airway for hysteroscopy | "Appropriately fasted" | Regurgitation of gastric contents | Tirzepatide recently started |
| Yeo *et al.*[47] | GLP-1 receptor agonist users (n = 46,935) *vs.* nonusers (n = 916,249) | Retrospective database cohort | Type 2 diabetes, obesity | Upper endoscopies ± colonoscopies | Not reported | Increase in aspiration pneumonia in GLP-1 receptor agonist users *vs.* nonusers (hazard ratio, 1.33; $P = 0.036$) | -GLP-1 receptor agonist users defined as taking medication for more than 6 mo and two refills within 6 mo before procedures -Increased hazard ratio for propofol-assisted endoscopies (hazard ratio, 1.49; $P = 0.014$) *vs.* no propofol (hazard ratio, 1.31; $P = 0.310$) GLP-1 receptor agonist users at increased risk with upper endoscopy (hazard ratio, 1.48; $P = 0.002$) and combined upper and lower endoscopies (hazard ratio, 2.26; $P = 0.007$) but not lower endoscopy (hazard ratio, 0.56; $P = 0.160$) |
| Anazco *et al.*[19] | GLP-1 receptor agonist users (n = 4,134) | Retrospective | Type 2 diabetes, obesity | Upper endoscopies | Not reported | Two episodes of aspiration pneumonia, both with monitored anesthesia care | Rates of aspiration similar to historical cohort 4.6 per 10,000 *vs.* 4.8/10,000 |
| Dixit *et al.*[20] | GLP-1 receptor agonist users (n = 3,502) *vs.* nonusers (n = 20,177) | Retrospective database | Type 2 diabetes | Emergency surgeries | Not reported | Aspiration events 3.5% in GLP-1 receptor agonist users *vs.* 4.0% in nonusers (adjusted odds ratio, 1.03; $P = 0.80$) | No increased aspiration with emergency surgeries |
| Klonoff *et al.*[48] | GLP-1 receptor agonist users (n = 2,256) *vs.* nonusers (n = 11,405) | Retrospective database, 1:1 matching cohorts | Type 2 diabetes | Surgeries with general endotracheal anesthesia | Not reported | GLP-1 receptor agonist users *vs.* nonusers had lower risk for postoperative decelerated gastric emptying outcomes (odds ratio, 0.81) and aspiration/ pneumonitis (odds ratio, 0.78) | |
| Barlowe *et al.*[49] | 274,211 upper endoscopies, 15,119 GLP-1 receptor agonist users, 14,407 DPP4 inhibitor users | Retrospective database | Type 2 diabetes | Upper endoscopy | Not reported | When comparing GLP-1 receptor agonist users to DPP4 inhibitor users, crude relative risks of aspiration (0.67), aspiration pneumonia (0.95), pneumonia (1.07), or respiratory failure (0.75) were not higher in patients prescribed GLP-1 receptor agonist | |

(*Continued*)

**Table 3.** (Continued)

| Author | GLP-1 Receptor Agonist (No. of Patients) | Study Type | Indication for GLP-1 Receptor Agonist | Procedure/ Anesthetic | Length of Fasting | Findings | Comments |
|---|---|---|---|---|---|---|---|
| **Residual gastric content by ultrasound or upper endoscopy** | | | | | | | |
| Fujino *et al.*[8] | Semaglutide | Case report | Obesity, type 2 diabetes | Upper endoscopy with monitored anesthesia care<br>Second endoscopy | 10 h<br>36 h (liquids only) | Residual gastric contents present after overnight fast<br>No residual gastric contents | Semaglutide 0.25 mg started 1 mo before procedure<br>Semaglutide 0.25 mg started 2 mo before procedure, last dose 7 days before procedure |
| Queiroz *et al.*[50] | Semaglutide | Case report | Obesity | Computer tomography | 9 h (solids and liquids) | Solid gastric contents seen on computed tomography | Semaglutide 0.5 mg started 6 days before procedure |
| Hodgson *et al.*[51] | Semaglutide | Case report | Type 2 diabetes | Gastric ultrasound | 10 h | Residual gastric contents present after overnight fast | Semaglutide 2 mg 3 days before procedure |
| Kittner *et al.*[10] | Semaglutide (n = 3) | Case series | Obesity, type 2 diabetes | Gastric ultrasound preinduction of general anesthesia | 10 h | Residual gastric contents by gastric ultrasound after 10 h fast | Semaglutide taken 1–6 days before procedure |
| Stark *et al.*[11] | GLP-1 receptor agonist users (n = 59) *vs.* nonusers (n = 118) | Retrospective, single-center | Type 2 diabetes | Upper endoscopy | Not reported | Residual gastric contents in 4.6% of GLP-1 receptor agonist users and 1.7% in no GLP-1 receptor agonist users; $P = 0.08$ | |
| Silveira *et al.*[12] | Semaglutide (n = 33) *vs.* no semaglutide (n = 371) | Retrospective, single-center | Obesity, type 2 diabetes | Upper endoscopy | 9 h for clear fluids and 14 h for solids | Residual gastric contents in semaglutide (24.2%) *vs.* non-semaglutide (5.1%) users; $P < 0.001$ | Colonoscopy found to protect against residual gastric contents |
| Sherwin *et al.*[13] | Semaglutide (n = 10) *vs.* no semaglutide (n = 10) | Prospective, single-center | Obesity | Gastric ultrasound | 8 h | Residual gastric contents in semaglutide (70%) and no semaglutide (20%) users; $P = 0.005$ | 90% taking semaglutide < 8 wk |
| Kobori *et al.*[14] | GLP-1 receptor agonist users (n = 205) *vs.* nonusers (n = 205) | Retrospective, single-center | Type 2 diabetes | Upper endoscopy | >12 h | Residual gastric contents in GLP-1 receptor agonist (5.4%) *vs.* no GLP-1 receptor agonist (0.49%) users; $P = 0.004$ | Residual gastric contents with liraglutide once daily 1.8 mg (n = 2), dulaglutide 0.75 mg (n = 5), semaglutide 0.5 mg (n = 2), and semaglutide 1.0 mg (n = 2) |
| Nadeem *et al.*[15] | GLP-1 receptor agonist users (n = 933) *vs.* nonusers (n = 34,261) | Retrospective, single-center | Obesity, type 2 diabetes | Upper endoscopy | Not reported | Residual gastric contents with GLP-1 receptor agonist 13.6% *vs.* no GLP-1 receptor agonist 2.3%; $P < 0.0001$<br>Aborted endoscopic gastroduodenoscopy 1.5% with GLP-1 receptor agonist *vs.* 0.3% if no GLP-1 receptor agonist; $P < 0.0001$ | |
| Firkins *et al.*[16] | GLP-1 receptor agonist users (n = 1,512) | Single-center, retrospective | Obesity, type 2 diabetes | Upper endoscopy ± colonoscopy | Not reported | Residual gastric contents in 9.4% of patients, mostly solids (7.4%) | Colonoscopy associated with reduced residual gastric contents (adjusted odds ratio, 0.34; $P < 0.001$) |
| Garza *et al.*[17] | GLP-1 receptor agonist users (n = 306) *vs.* nonusers (n = 306) | Retrospective, case–control | Obesity, type 2 diabetes | Upper endoscopy ± colonoscopy | Not reported | Residual gastric contents with GLP-1 receptor agonist 14% *vs.* 4% for nonusers, ($P <$ 0.01), especially in patients with type 2 diabetes (14% *vs.* 4%; $P < 0.01$), taking insulin (17% *vs.* 5%; $P < 0.01$), and with type 2 diabetes complications (15% *vs.* 2%; $P < 0.01$) | Less residual gastric contents after prolonged fasting and clear liquids for concurrent colonoscopy (2% *vs.* 11%; $P < 0.01$) and in patients with afternoon procedures (4% *vs.* 11%; $P < 0.01$) |
| Wu *et al.*[18] | GLP-1 receptor agonist users (n = 90) *vs.* nonusers (n = 102) | Retrospective | Obesity, type 2 diabetes | Upper endoscopy | 16 h in both groups | Residual gastric contents 19% in GLP-1 receptor agonist users *vs.* 5% in nonusers (adjusted odds ratio, 5.8; $P = 0.004$) | |

(*Continued*)

**Table 3.** (Continued)

| Author | GLP-1 Receptor Agonist (No. of Patients) | Study Type | Indication for GLP-1 Receptor Agonist | Procedure/ Anesthetic | Length of Fasting | Findings | Comments |
|---|---|---|---|---|---|---|---|
| Sen *et al.*[21] | GLP-1 receptor agonist users (n = 62) *vs.* nonusers (n = 62) | Prospective, single-center | Obesity, type 2 diabetes | Ultrasound before induction of anesthesia | 13–15 h for solids (both groups)<br>3–6 h for liquids (both groups) | Residual gastric contents 56% in GLP-1 receptor agonist users *vs.* 19% in nonusers | No association between duration of discontinuation and increased residual gastric contents (adjusted odds ratio, 0.86), risk elevated even after 7-days discontinuation<br>No association between GLP-1 receptor agonist type and increased residual gastric contents |
| Chapman *et al.*[52] | GLP-1 receptor agonist users (n = 84) *vs.* nonusers (n = 84) | 1:1 matched controlled | Obesity, type 2 diabetes | Upper endoscopy | > 10 h for solids<br>> 2 h for liquids | Residual gastric contents in the GLP-1 receptor agonist group (13.1%) *vs.* nonusers (4.8%); adjusted odds ratio, 4.62 ($P = 0.025$) | Mostly monitored anesthesia care<br>No aspiration events |
| Maselli *et al.*[53] | GLP-1 receptor agonist users (n = 57) | Retrospective | Obesity, type 2 diabetes | Upper endoscopy | > 24 h for solids<br>> 12 h for liquids | No residual gastric contents, pulmonary aspiration, gastroesophageal regurgitation, or hypoxia | All patients continued GLP- 1 receptor agonist |

DPP4, dipeptidyl peptidase 4; GLP-1, glucagon like peptide-1.

a 48% decrease in minimum concentration expected before the next planned dose 7 days later. Delaying the dose 5 days causes minimum semaglutide concentrations to be 37% lower and the maximum concentration after the next dose to be 14% higher compared with the same subject at a normal weekly steady state. In both cases, the nadir of the semaglutide concentrations is higher than the mean concentration at steady state of a similar patient taking 0.5 mg weekly, and closer to regular steady state after 3 weeks[91] (fig. 2).

- Similarly, if a dose of dulaglutide or tirzepatide is missed, there is residual circulating GLP-1 receptor agonist. Moreover, if a dose of dulaglutide is not taken within 3 days or if tirzepatide is held for 4 days, there are transient 20% higher concentrations after the subsequent doses of the GLP-1 receptor agonist[25,92] (figs. 3 and 4).
- Package inserts advise skipping the missed dose and administering the GLP-1 receptor agonist on the regularly scheduled day if fewer than 3 days remain until the next dose for exenatide, dulaglutide, or tirzepatide, or fewer than 2 days for semaglutide.[93]

- More importantly, clinical data confirm that even when a GLP-1 receptor agonist dose is omitted, some patients have residual gastric contents on the day of procedure while following standard fasting guidelines.[89]
  - A prospective study of 124 patients presenting for surgeries found ultrasonographic confirmation of increased gastric contents defined by the presence of solids, thick liquids, or more than 1.5 ml/kg clear liquids in patients taking GLP-1 receptor agonists. Interestingly, there was no association between the duration of drug interruption and the prevalence of increased gastric contents, including in some patients who had stopped their drugs more than 7 days before surgery.[21]
  - Another study of 404 patients found no relationship between the interval interruption of semaglutide and the presence of residual gastric contents in patients having endoscopies. The interruption intervals of semaglutide in patients without retained gastric contents were 10 days (6 to 15) compared to 11 days (7.75 to 12.5) in those with delayed emptying ($P = 0.67$).[12]

Considerations of *risks* associated with stopping GLP-1 receptor agonists are the following:

- In patients with diabetes mellitus prescribed GLP-1 receptor agonists, no glycemic data are available on the effects of stopping GLP-1 receptor agonists. It is likely that glycemia control will deteriorate, especially in those with poor control, requiring multidrug regimens, taking insulin, or on high doses of antihyperglycemics. Moreover, acute hyperglycemia slows gastric emptying, so it is possible that this will negate the benefit of stopping the drugs.[94]

**Table 4.** Studies Assessing Gastric Emptying in Patients on GLP-1 Receptor Agonists

| Reference | Drug | Indication | Design | No. of Patients | Protocol Used | Test Used | Results |
|---|---|---|---|---|---|---|---|
| **Gastric emptying for solids in patients taking short-acting GLP-1 receptor agonists** | | | | | | | |
| Acosta *et al.* 2015[54] | Exenatide | Obesity | Randomized controlled trial, double-blinded, single-center | 20 | Exenatide 5 μg subcutaneously twice daily *vs.* placebo for 30 d | Nuclear scintigraphy (solid meal) | Delayed gastric emptying at 30 days in exenatide group compared to placebo. $T_{1/2}$ was 187 min with exenatide *vs.* 86 min with placebo ($P < 0.001$). |
| Linnebjerg *et al.* 2008[55] | Exenatide | Type 2 diabetes | Randomized controlled trial, single-blinded | 17 | Exenatide 5 μg, exenatide 10 μg, or placebo for 5 d | Nuclear scintigraphy (solid meal) | After 5 d, $T_{1/2}$ of solids was 60 min for placebo, 111 min for exenatide 5 μg, and 169 min for exenatide 10 μg (both *vs.* placebo; $P < 0.01$). Delayed gastric emptying for both doses of exenatide. |
| Kuwata *et al.* 2021[56] | Dulaglutide Liraglutide Lixisenatide | Type 2 diabetes | Single-arm, prospective, observational | 18 | Lixisenatide 10 μg subcutaneously daily week 1, 15 μg daily week 2, and 20 μg on the day of the meal test at week 2 and thereafter up to 12 wk Liraglutide 0.3 mg daily in week 1, 0.6 mg in week 2, and 0.9 mg on the day of the meal test in week 2 and thereafter up to 12 wk Dulaglutide 0.75 mg weekly for 12 wk | $^{13}$C-acetate breath test | $T_{1/2}$ extended by lixisenatide, at weeks 2 and 12 ($P < 0.05$). |
| Quast *et al.* 2020[57] | Liraglutide Lixisenatide | Type 2 diabetes | Randomized, bicentric, investigator-blinded, parallel-group study | 57 | Lixisenatide 10 μg subcutaneously daily for 1 wk, followed by 20 μg subcutaneously for 9 wk Liraglutide 0.6 mg once daily for week 1, 1.2 mg once daily for week 2, followed by 1.8 mg once daily for 8 wk | $^{13}$C-sodium octanoate breath test | At 10 wk, $T_{1/2}$ was delayed by 52 min with lixisenatide ($P = 0.0065$) compared to baseline. |
| Lorenz *et al.* 2013[58] | Lixisenatide | Type 2 diabetes | Randomized controlled trial, double-blinded, parallel-group study | 43 | Lixisenatide 5 μg subcutaneously and increased by 2.5 μg every 5 days to maximum of 20 μg daily *vs.* placebo for 8 wk | $^{13}$C-octanoic acid breath test | $T_{1/2}$ from baseline to day 28 was 211.5 min (delayed) for lixisenatide *vs.* - 24.1 min for placebo ($P = 0.0031$). |
| Meier *et al.* 2020[59] | Lixisenatide | Type 2 diabetes | Randomized controlled trial, open-label with two treatment regimens (4 wk of monotherapy with either lixisenatide or glargine insulin and another 4 wk of combination therapy with both medications) | 20 | Lixisenatide 10 μg (30 min before breakfast) initially, and after 2 wk increased to 20 μg if tolerated Glargine insulin at bedtime titrated to achieve glucose concentrations 4.4–5.6 mM | $^{13}$C-octanoic acid breath test | $T_{1/2}$ of test prolonged to 187 min for lixisenatide + glargine insulin ($P < 0.001$) and 168 min for lixisenatide alone ($P = 0.002$) *vs.* 87 min at baseline. |
| Meier *et al.* 2015[60] | Liraglutide Lixisenatide | Type 2 diabetes | Randomized controlled trial, open-label, multicenter | 94 | Lixisenatide 20 μg subcutaneously daily, liraglutide 1.2 mg subcutaneously or 1.8 mg daily combined with glargine insulin for 8 wk | $^{13}$C-sodium octanoate breath test | Gastric emptying delayed at 8 wk. $T_{1/2}$ was 537 min for lixisenatide *vs.* 169 min at baseline ($P < 0.001$). |
| **Gastric emptying for solids in patients taking long-acting GLP-1 receptor agonists** | | | | | | | |
| Jones *et al.* 2020[61] | Exenatide weekly | Obesity | Randomized controlled trial | 32 | Exenatide 2 mg weekly or placebo for 8 wk | Nuclear scintigraphy (solid meal) | After 8 wk, there was increased retention at 100 min with exenatide *vs.* placebo (52% *vs.* 36%; $P < 0.02$). |

(*Continued*)

**Table 4.** (Continued)

| Reference | Drug | Indication | Design | No. of Patients | Protocol Used | Test Used | Results |
|---|---|---|---|---|---|---|---|
| Maselli *et al.* 2022[62] | Liraglutide | Obesity | Randomized controlled trial | 130 | Liraglutide 0.6 mg daily, escalated by 0.6 daily every week to 3 mg subcutaneously daily for a total of 16 wk | Nuclear scintigraphy (solid meal) | $T_{1/2}$ increased with liraglutide at 5 and 16 wk (both $P < 0.001$) *vs.* placebo and increased fasting gastric volume ($P = 0.01$) at 16 wk. |
| Quast *et al.* 2020[57] | Liraglutide Lixisenatide | Type 2 diabetes | Randomized, bicentric, investigator-blinded, parallel-group study | 57 | Lixisenatide 10 μg subcutaneously daily for 1 wk, followed by 20 μg subcutaneously for 9 wk<br>Liraglutide 0.6 mg once daily for week 1, 1.2 mg once daily for week 2, followed by 1.8 mg once daily for 8 wk | $^{13}$C-sodium octanoate breath test | At 10 wk, $T_{1/2}$ was increased by 25 min with liraglutide ($P = 0.025$) compared to baseline. |
| Kuwata *et al.* 2021[56] | Dulaglutide Liraglutide Lixisenatide | Type 2 diabetes | Single-arm, prospective, observational | 18 | Lixisenatide 10 μg subcutaneously daily week 1, 15 μg daily week 2, and 20 μg on the day of the meal test at week 2 and thereafter up to 12 wk<br>Liraglutide 0.3 mg daily in week 1, 0.6 mg week 2, and 0.9 mg on the day of the meal test week 2 and thereafter up to 12 wk<br>Dulaglutide 0.75 mg weekly for 12 wk | $^{13}$C-acetate breath test | $T_{1/2}$ nonsignificantly increased by liraglutide at 2 wk and largely unaffected by liraglutide and dulaglutide at 2 and 12 wk. |
| Meier *et al.* 2015[60] | Liraglutide Lixisenatide | Type 2 diabetes | Randomized controlled trial, open-label, multicenter | 94 | Lixisenatide 20 μg subcutaneously daily, liraglutide 1.2 mg or 1.8 mg subcutaneously daily combined with glargine insulin for 8 wk | $^{13}$C-sodium octanoate breath test | Gastric emptying delayed at 8 wk with liraglutide.<br>$T_{1/2}$ was 259 min for 1.2 mg liraglutide and 209 min for 1.8 mg liraglutide *vs.* 164 min at baseline ($P < 0.001$). |
| Nagai *et al.* 2014[63] | Liraglutide | Type 2 diabetes | Prospective | 16 | Liraglutide initiated at 0.3 mg daily, and increased by 0.3 mg every 3 days to maximum 0.9 mg for 7 d | $^{13}$C-acetate breath test | $T_{1/2}$ after liraglutide increased by 31 ± 4 min *vs.* baseline ($P < 0.01$) in some patients (delayers) compared to 2 ± 3 min *vs.* baseline ($P = 0.60$) in others (nondelayers). |
| Halawi *et al.* 2017[64] | Liraglutide | Obesity | Randomized controlled trial, double-blinded, single-center | 21 | Liraglutide titrated by 0.6 mg/wk for 5 wk to 3.0 mg subcutaneously daily, continued until week 16 or placebo | Nuclear scintigraphy (solid meal) | Gastric emptying of solids from baseline to 5 wk more delayed with liraglutide (median 70 min) *vs.* placebo (median 4 min; $P < 0.0001$).<br>Gastric emptying of solids $T_{1/2}$ change from baseline to 16 wk delayed with liraglutide (median 30.5 min) *vs.* placebo (median -1 min; $P = 0.025$). |
| Nakatani *et al.* 2017[65] | Liraglutide | Type 2 diabetes | Single-center, observational | 14 | Liraglutide 0.3 mg subcutaneously daily for a week, 0.6 mg daily for a week, and 0.9 mg daily for 2 wk | Transit time of capsule endoscopy | Gastric transit time (n = 14) 1:11:53 ± 1:03:17 h at baseline and 1:45:46 ± 1:40:46 h after liraglutide 1 wk after final dose of 0.9 mg ($P = 0.16$).<br>Patients without diabetic neuropathy (n = 7) had gastric transit of 1:01:30 ± 0:52:59 h at baseline and 2:33:29 ± 1:37:24 h after liraglutide ($P = 0.03$).<br>Patients with diabetic neuropathy y (n = 7) had gastric transit of 1:12:36 ± 1:04:30 h at baseline and 0:48:40 ± 0:32) 52 h after liraglutide ($P = 0.19$). |

(*Continued*)

**Table 4.** (Continued)

| Reference | Drug | Indication | Design | No. of Patients | Protocol Used | Test Used | Results |
|---|---|---|---|---|---|---|---|
| Jensterle *et al.* 2023[66] | Semaglutide | Obesity | Single-blinded, placebo-controlled | 20 | Semaglutide 1.0 mg subcutaneously weekly or placebo for 12 wk | Nuclear scintigraphy (solid food) | Gastric contents increased 3.5% at 1 h, 25.5% at 2 h, 38.0% at 3 h, and 30.0% at 4 h with semaglutide. Four hours after ingestion, 37% of solids retained with semaglutide *vs.* placebo ($P = 0.002$). $T_{1/2}$ significantly increased with semaglutide *vs.* placebo (171 *vs.* 118 min; $P < 0.001$). |
| **Gastric emptying for liquids in patients taking short-acting GLP-1 receptor agonists** | | | | | | | |
| Cervera *et al.* 2008[67] | Exenatide | Type 2 diabetes, obesity | Single-center, placebo-controlled | 12 | Exenatide IV (0.05 μg/min 15 min before meals, decreased to 0.025 μg/min 45 min after meals) *vs.* placebo, treatment repeated three times, 2–4 wk apart | Acetaminophen (with solid meal) | Delay in gastric emptying after 6 h with exenatide reflected by a 58% decrease in mean plasma acetaminophen concentration ($P < 0.001$) *vs.* placebo. |
| DeFronzo *et al.* 2008[68] | Exenatide | Type 2 diabetes | Randomized controlled trial, double-blinded, crossover, multicenter | 95 | Exenatide 5 μg twice daily for 1 wk, then 10 μg twice daily for 1 wk or sitagliptin daily for 2 wk | Acetaminophen (with solid meal) | After 2 wk, delayed gastric emptying with exenatide *vs.* sitagliptin ($P < 0.0001$), measured up to 4 h. |
| Drucker *et al.* 2008[69] | Exenatide | Type 2 diabetes, obesity | Randomized, open-label | 50 | Exenatide 2.0 mg subcutaneously weekly in 26 patients or subcutaneously twice daily or exenatide 5 μg subcutaneously twice daily, titrated to 10 μg twice daily after 28 d in 24 patients for 14 wk | Acetaminophen (with solid meal) | Gastric emptying at week 14 delayed compared to baseline with exenatide twice daily measured up to 5 h. |
| Kolterman *et al.* 2005[70] | Exenatide | Type 2 diabetes | Randomized controlled trial, single-blinded, placebo-controlled | 8 | Exenatide daily: 0.02 μg/kg, 0.05 μg/kg, and 0.10 μg/kg or placebo on 4 consecutive days | Acetaminophen (liquid meal) | Dose-dependent slowing of gastric emptying compared to placebo ($P = 0.0011$), measured up to 2 h. |
| Juel *et al.* 2020[71] | Lixisenatide | Status post pancreatectomy | Randomized controlled trial, double-blinded, crossover study | 24 | Lixisenatide 20 μg subcutaneously or placebo, one single dose | Acetaminophen (liquid meal) | Lixisenatide reduced gastric emptying *vs.* placebo in both the totally pancreatectomized ($P < 0.001$) and the controls ($P < 0.001$). |
| Becker *et al.* 2015[72] | Lixisenatide | Healthy | Randomized controlled trial, open-label, crossover, single-center | 20 | Lixisenatide 2.5, 5, 10, or 20 μg subcutaneously for one dose with 2–7-d washout period | Acetaminophen (liquid meal) | Gastric emptying at 1 h delayed at doses >5 μg ($P < 0.05$). |
| Jones *et al.* 2019[73] | Lixisenatide | Healthy, type 2 diabetes | Randomized controlled trial, double-blinded, crossover study | 30 | Lixisenatide 10 μg subcutaneously or placebo on 2 separate days | Nuclear scintigraphy (25% glucose drink) | Delayed gastric emptying at 3 h in both healthy subjects and subjects with type 2 diabetes with lixisenatide compared to placebo. |
| Jalleh *et al.* 2020[74] | Lixisenatide | Healthy, type 2 diabetes | Randomized controlled trial, double-blind, placebo-controlled, crossover design | 30 | Lixisenatide 10 μg subcutaneously or placebo on 2 separate days | Nuclear scintigraphy (25% glucose drink) | Proximal stomach retention in healthy group at 3 h was 6.6% with placebo *vs.* 40.9% with lixisenatide ($P < 0.001$) and in the type 2 diabetes group was 6.3% with placebo *vs.* 34.8% with lixisenatide ($P < 0.001$). Distal stomach retention at 3 h in healthy group was 9.4% with placebo *vs.* 18.6% with lixisenatide ($P < 0.001$) and in type 2 diabetes was 8.2% with placebo *vs.* 19.6% with lixisenatide ($P < 0.001$). |

(*Continued*)

**Table 4.** (Continued)

| Reference | Drug | Indication | Design | No. of Patients | Protocol Used | Test Used | Results |
|---|---|---|---|---|---|---|---|
| Rayner *et al.* 2020[75] | Lixisenatide | Type 2 diabetes | Randomized controlled trial | 30 | Lixisenatide 20 μg subcutaneously daily or placebo for 8 wk | Nuclear scintigraphy (25% glucose drink) | Delayed gastric emptying at 2 h and 4 h with lixisenatide at 8 wk *vs.* placebo ($P < 0.001$). |
| Kovoor *et al.* 2024[76] | Lixisenatide | Type 2 diabetes | Randomized controlled trial | 30 | Lixisenatide 20 μg subcutaneously daily or placebo for 8 wk | Nuclear scintigraphy (25% glucose drink) | Delayed gastric emptying at 4 h with lixisenatide at 8 wk *vs.* placebo ($P < 0.0001$). |
| **Gastric emptying for liquids in patients taking long-acting GLP-1 receptor agonists** | | | | | | | |
| Jones *et al.* 2020[61] | Exenatide weekly | Obesity | Randomized controlled trial | 32 | Exenatide 2 mg weekly or placebo for 8 wk | Nuclear scintigraphy (radiolabeled glucose with solid meal) | After 8 wk, exenatide slowed gastric emptying of liquids ($P = 0.01$) measured up to 2 h. |
| Drucker *et al.* 2008[69] | Exenatide weekly | DM, obesity | Randomized, open-label | 50 | Exenatide 2.0 mg subcutaneously weekly in 26 patients or subcutaneously twice daily or exenatide 5 μg subcutaneously twice daily, titrated to 10 μg twice daily after 28 d in 24 patients for 14 wk | Acetaminophen (with solid meal) | Gastric emptying at week 14 not delayed with weekly dosing when compared to baseline, suggesting tachyphylaxis, measured up to 5 h. |
| Barrington *et al.* 2011[77] | Dulaglutide | Type 2 diabetes | Randomized controlled trial, double-blinded, multicenter | 43 | Weekly placebo *vs.* dulaglutide subcutaneously 0.05 mg (n = 3), 0.3 mg (n = 6), 1 mg (n = 5), 3 mg (n = 3), 5 mg (n = 9), or 8 mg for 5 wk | Acetaminophen (with solid meal) | Significant delay in gastric emptying with 5 mg dose after recent start of dulaglutide. |
| Degn *et al.* 2004[78] | Liraglutide | Type 2 diabetes, obesity | Randomized controlled trial, double-blinded, crossover | 13 | Liraglutide 6 μg/kg subcutaneously or placebo for 9 days | Acetaminophen (with solid meal) | After 8 days, no change in gastric emptying with liraglutide *vs.* placebo measured up to 2 h. |
| Dejgaard *et al.* 2016[79] | Liraglutide | Obesity, type 1 diabetes | Randomized controlled trial | 10 | Liraglutide 0.6 mg subcutaneously daily, increased to 1.2 mg subcutaneously daily after 1 wk, then to 1.8 mg daily after 1 wk or placebo for 3 wk | Acetaminophen (with liquid meal) | Gastric emptying delayed after 3 wk of liraglutide (19.9 min; $P = 0.0412$), but no difference after 24 wk of treatment (–1.5 min; $P = 0.8793$). |
| Flint *et al.* 2011[80] | Liraglutide | Type 2 diabetes | Randomized controlled trial, double-blinded, single-center | 18 | Liraglutide 0.6 mg subcutaneously daily, increased to 1.2 mg subcutaneously daily after 1 wk, then to 1.8 mg daily after 1 wk or placebo for 3 wk | Acetaminophen (with solid meal) | Gastric emptying delayed with 1.2 mg dose ($P < 0.001$) but not significant for 0.6 mg or 1.8 mg, measured greater than 5 h *vs.* placebo at end of each dosing change.<br>Gastric emptying delayed in the first hour, with 1.2 mg ($P < 0.001$) and 1.8 mg ($P = 0.028$). |
| Horowitz *et al.* 2012[81] | Liraglutide | Type 2 diabetes | Randomized controlled trial, double-blinded, incomplete crossover, two centers | 46 | Participants randomized to two of three arms for 4 wk, with a 3-wk washout; liraglutide followed by placebo, placebo followed by glimepiride, glimepiride followed by liraglutide<br>Liraglutide started at 0.6 mg subcutaneously daily, escalated by 0.6 mg increments weekly to a maximum dose of 1.8 mg daily, maintained for 2 wk; glimepiride started at 1 mg daily for 1 wk, then titrated to 2–4 mg daily per renal function | Acetaminophen (with liquid meal) | At end of 4 wk gastric emptying delayed in liraglutide compared to control groups.<br>($P < 0.001$), measured at 1 h and 5 h.<br>Acetaminophen maximum serum concentrations 20% lower with liraglutide *vs.* placebo and 15% lower with liraglutide than glimepiride ($P \leq 0.006$ for both). |

(*Continued*)

**Table 4.** (Continued)

| Reference | Drug | Indication | Design | No. of Patients | Protocol Used | Test Used | Results |
|---|---|---|---|---|---|---|---|
| van Can *et al.* 2014[82] | Liraglutide | Obesity | Randomized controlled trial, single-center | 49 | Two randomly chosen treatment periods of 5 wk each, with 6–8 wk washouts<br>Liraglutide 1.8 mg subcutaneously daily, liraglutide 3.0 mg subcutaneously daily, or placebo | Acetaminophen (with solid meal) | No difference in gastric emptying between either liraglutide doses and placebo, measured at 5 h at the end of each 5-wk period.<br>Delayed gastric emptying from both liraglutide doses over the first hour: 23% less with liraglutide 3.0 mg *vs.* placebo ($P = 0.007$), 13% less with liraglutide 1.8 mg *vs.* placebo ($P = 0.14$). |
| Saxena *et al.* 2021[83] | Liraglutide | Obesity | Randomized controlled trial | 61 | Liraglutide initiated at 0.6 mg subcutaneously daily and escalated by 0.6 mg/wk to a maximum of 3.0 mg/d or placebo for a total of 6 wk | Acetaminophen (with solid meal) | Delayed gastric emptying at 3 and 6 wk with liraglutide at 1 h ($P = 0.0348$) and 5 h ($P = 0.0152$). |
| Hjerpsted *et al.* 2018[84] | Semaglutide | Obesity | Randomized controlled trial, double-blinded, two-period, crossover | 30 | Semaglutide 0.25 mg subcutaneously weekly for 4 wk, 0.5 mg weekly for 4 wk, then 1.0 mg weekly for 4 wk or placebo | Acetaminophen (solid meal) | Gastric emptying delayed in first hour with semaglutide at 12 wk.<br>No differences in gastric emptying at 5 h for semaglutide *vs.* placebo. |
| Dahl *et al.* 2021[85] | Semaglutide oral | Type 2 diabetes | Randomized, double-blinded, single-center | 15 | Semaglutide daily orally, at 3 mg daily for 4 wk, then 7 mg daily for 4 wk, and then 14 mg daily for 4 wk followed by placebo after 4–9 washout weeks, or *vice versa*, during two consecutive 12-wk periods | Acetaminophen (solid meal) | Gastric emptying delayed by 31% with semaglutide *vs.* placebo during first postprandial hour, but not significantly different at 5 h. |
| Friedrichsen *et al.* 2021[86] | Semaglutide | Obesity | Randomized controlled trial | 72 | Semaglutide subcutaneously 0.25 mg weekly for 4 wk, escalated to 0.5 weekly for 4 wk, 1 mg weekly for 4 wk, 1.7 mg weekly for 4 wk, and 2.4 mg weekly for 5 wk or placebo for 20 wk | Acetaminophen (solid meal) | Gastric emptying not delayed with semaglutide 2.4 mg *vs.* placebo at week 20 ($P = 0.12$). |
| Urva *et al.* 2020 [87] | Tirzepatide | Healthy, type 2 diabetes | Investigator-blinded, three parts: single-ascending dose and 4-wk multiple-ascending doses in healthy participants, followed by a 4-wk multiple-doses phase 1b proof of concept in participants with type 2 diabetes | 86 (n = 33 healthy, n = 53 with type 2 diabetes) | Tirzepatide 0.5 mg, 1.5 mg, 4.5 mg, 5 mg, 10 mg, or 15 mg subcutaneously weekly (4 wk per dose) | Acetaminophen (solid meal) | Gastric emptying delayed with tirzepatide ≥ 4.5 and ≥ 5 mg after a single dose. Effect diminished after multiple doses of tirzepatide in healthy group.<br>Gastric emptying delayed after multiple doses with escalation of tirzepatide 5/5/10/10 or 5/5/10/15 mg in type 2 diabetes group. |

Adapted with permission from Maselli and Camilleri, Adv Exp Med Biol 2021; 1307:171–92).[88]
GLP-1, glucagon-like peptide-1; IV, intravenous; $T_{1/2}$, time to half gastric emptying.

- Patients taking high doses of GLP-1 receptor agonists (more common in obese patients, but also in patients with diabetes) and those experiencing severe symptoms at initiation or during escalation of treatment are at high risk of adverse gastrointestinal effects when doses are missed and then restarted.[93] These patients often need to be started on a lower dose of drug to mitigate side effects. However, this is logistically difficult since some of these medications (*e.g.*, tirzepatide, dulaglutide) are packaged in prefilled syringes, and patients are provided with precise doses monthly. In contrast, semaglutide pens allow adjustment of doses.[93]

Both pharmacokinetic and clinical data indicate that short interruptions of long-acting GLP-1 receptor agonist (*i.e.*, one half-life) are not sufficient to ensure complete

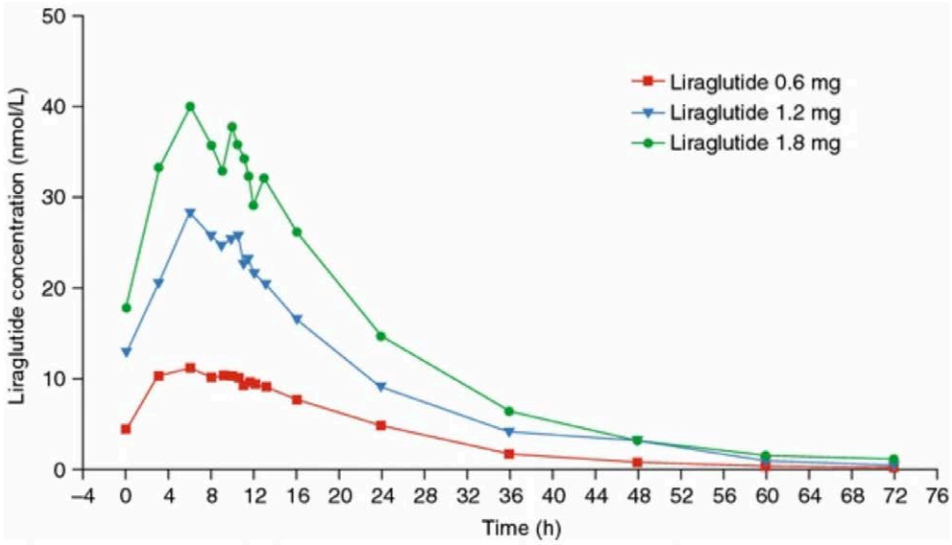


**Fig. 1.** Steady-state concentration-time curve of liraglutide after last dose (day 21). From Jacobsen *et al.* Clin Pharmacokinet 2016; 55:657–72.[24]

clearance of the drug. While no data are available on gastric emptying from residual GLP-1 receptor agonist concentrations, it is likely that there is no complete dissipation of the effect. The longer duration of interruption needed (*i.e.*, 4 or 5 half-lives) is impractical, potentially harmful, and not patient-centric.

Moreover, there are data suggesting safety of continuation of GLP-1 receptor agonists periprocedurally. A study in patients having endoscopy while continuing their medications and following a modified fasting regimen reported no increased gastric volumes and no aspiration events.[53]

Symptomatic patients describing severe gastrointestinal symptoms may represent a special category where the medication regimen can be interrupted or dose de-escalated. However, even in these patients, current guidelines recommend dietary interventions such as small frequent meals and consumption of bland foods as a first-line intervention.[95,96] Medication adjustments are recommended only when symptoms do not resolve.[95,96]

## Role of Fasting

Current guidance suggests that the standard fasting time is sufficient to mitigate aspiration risk in patients taking GLP-1 receptor agonists.[22] However, this approach is questionable based on clinical data (table 3).

Considerations for *solid* fasting times are the following:

- Many patients found to have residual gastric contents on the day of their procedures have observed the standard ASA fasting times.[12,21] In these studies, despite interrupting GLP-1 receptor agonist for more than 7 days, patients had retained gastric contents.[12,21]
- Data from a case control study showed lower rates of persistent stomach contents in patients having afternoon procedures with prolonged fasting compared to those having procedures in the morning (4% *vs.* 11%; $P < 0.01$).[17]
- Several studies reveal that patients having colonoscopies (with or without upper endoscopies) have a lower incidence of retained gastric contents.[12,16,17,47] This is most likely due to the fact that patients having colonoscopies typically follow a clear liquid diet the day before the procedure, and less likely due to the concurrent bowel preparation.[97]

The evidence suggests that an extended fasting time for solids should be recommended for patients taking GLP-1 receptor agonists. Perhaps the best data in support of this approach come from a study of 57 patients having endoscopies where GLP-1 receptor agonists were not stopped. All of the patients followed a liquid diet for 24 h or more and were *nil per os* (nothing by mouth; NPO) for more than 12 h before their endoscopies. No patients had detectable residual gastric contents determined by endoscopy, and no aspiration events occurred.[53] Overall, there is clear evidence of delayed gastric emptying for solids irrespective of the type of GLP 1 receptor agonist preparation or duration of treatment, suggesting that a clear liquid diet for 24 h or more may be necessary for these patients.

At this time, the best duration of fasting from *liquids* is unclear because data are scarce and heterogeneous.

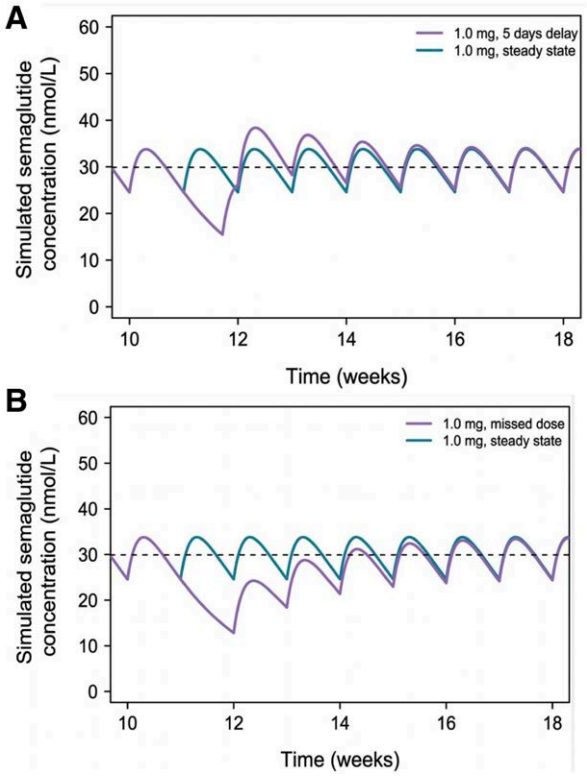


**Fig. 2.** Simulated semaglutide concentration profiles after missed or delayed doses. Data are simulated concentrations during once-weekly dosing at steady state concentrations with one missed dose at week 11 (*A*) and for a dose with a delay of 5 days at week 11 (*B*) compared with a steady state profile for semaglutide dosed at weekly intervals. Simulations are for a reference subject profile (non-Hispanic or Latino, white female, 65 yr, with a body weight of 85 kg, with normal renal function, and dosed in the abdomen with semaglutide 1.0 mg). From Carlsson Petri *et al.* Diabetes Ther 2018; 9:1533–47.[91]

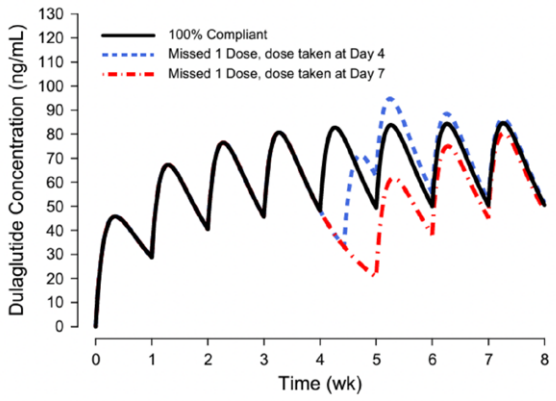


**Fig. 3.** Effects of missed doses on concentration–time profiles of dulaglutide. The pharmacokinetic model simulated dulaglutide concentration–time profiles after a once-weekly dose of 1.5 mg taken as prescribed (*solid black line*), with a dose being missed at midweek (*blue dashed line*) or with a dose being skipped (*red dotted–dashed line*). From Geiser *et al.* Clin Pharmacokinet 2016;55:625–34.[25] Used with permission.

- Various liquids empty from the stomach at different rates. High-caloric liquids (those containing fat or greater than 10% glucose) empty more slowly than water or low caloric clear liquids (10% glucose or less) in patients with normal gastric emptying.[98]
- Patients on short-acting preparations have delayed gastric emptying for liquids after weeks of treatments. Significant liquid intragastric content has been described at 4 h after 8 weeks of treatment with lixisenatide with consumption of high-caloric glucose–containing liquids.[73–76]
- In individual studies, patients on long-acting preparations in a maintenance phase at least 4 weeks from initiation seem to have slightly prolonged delays in gastric emptying for liquids in the first 1 to 2 h that normalize by 5 h.[84–86] However, in the majority of these studies, acetaminophen elixir was given after a solid meal, which likely confounds the data and may overestimate the delay (table 4).
- Patients who recently started or dose-escalated long-acting GLP-1 receptor agonist within the previous 4 weeks do not exhibit tachyphylaxis and may need more prolonged NPO fasting times. A study of 20 patients detected that 30% of the semaglutide group (most of whom had been on therapy for less than 4 weeks) compared to 90% of the controls were considered to have empty stomachs 2 h after drinking 12 oz of clear liquids in a supine position.[13] These findings corroborate other data on gastric emptying assessed by acetaminophen absorption.[87]
- A recently published meta-analysis did not show any significant delay in gastric emptying for liquids regardless of the GLP-1 receptor agonist. However, it did not include all of the studies, and there was heterogenicity in the reported measurements and in the nature of the meals coadministered with the acetaminophen.[90]

There are concerns that prolonged fasting for liquids is not patient friendly and counters the principles of enhanced recovery. High-caloric carbohydrate drinks have been shown to empty slower than water even in patients not taking GLP-1 receptor agonists. They are generally not recommended in patients with diabetes where the risks of hyperglycemia may outweigh their benefits.[99] They may be restricted for longer than 4 h in patients on GLP-1 receptor agonists for obesity, because their emptying is particularly delayed, especially by short-acting GLP-1 receptor agonist.[73–76]

Extended restriction periods for other non- or low-caloric clear liquids may not be advantageous or necessary for the majority of patients on maintenance doses of long-acting GLP-1 receptor agonists for more than 4 weeks.

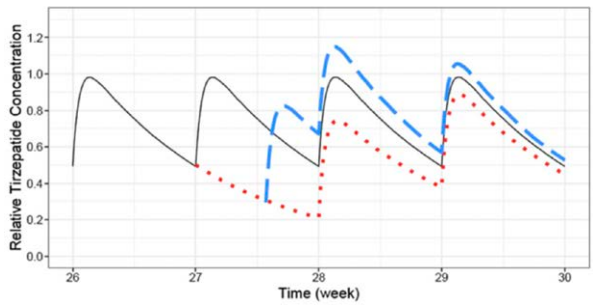


**Fig. 4.** Effects of delayed or missed dose on the steady-state concentration–time profile of tirzepatide. The pharmacokinetic model simulated tirzepatide concentration–time profiles after a once-weekly dose taken as prescribed (*solid black line*), with a dose being delayed until midweek (*blue dashed line*) or with a dose being skipped (*red dotted line*). From Schneck *et al.* CPT Pharmacometrics Syst Pharmacol 2024;13:494–503.[92] Used with permission.

However, not all patients exhibit tachyphylaxis.[61] The evidence suggests fasting for non- or low-caloric clear liquids for longer than current recommendations is necessary for patients taking long-acting preparations during initiation and dose escalation periods, and those on short-acting GLP-1 receptor agonists.

## Role of Gastric Ultrasonography

Point-of-care gastric ultrasonography has been used to identify patients taking GLP-1 receptor agonists who have residual gastric content preprocedurally.[10,13,21,51,99,100101] Training and achieving proficiency in gastric ultrasonography followed by wide adoption among anesthesiology clinicians will take some time. Most importantly, gastric ultrasonography only identifies those with retained gastric contents after they arrive for their procedures. It does not allow for timely interventions to avoid the risk of perioperative aspiration other than a change in the planned anesthetic or postponement of the procedure. A better approach is needed to ensure a majority of patients taking GLP-1 receptor agonists present without retained gastric contents preprocedurally and can avoid unnecessary anesthesia procedures such as rapid sequence induction and intubation, or aspiration on emergence from anesthesia. Gastric ultrasonography may be best suited for patients who are symptomatic or are asymptomatic without having observed prolonged fasting times.

## Summary

Emerging data point to the limitations of the current ASA consensus-based guidance for patients taking GLP-1 receptor agonists. It is becoming more obvious that interrupting GLP-1 receptor agonists as currently suggested may not offer much benefit, since a longer washout time is needed to resolve the effects on gastric emptying. Moreover, the current approach gives clinicians a false sense of security when proceeding with anesthesia, especially when a monitored anesthesia care or a standard general anesthesia induction technique is planned, as residual gastric contents may be present. Furthermore, the glycemia benefit and the perioperative effects of mitigating major adverse cardiovascular events may be lost with drug interruptions in patients with diabetes mellitus. Additionally, there is the possibility of renewed side effects when reinstating a high-dose GLP-1 receptor agonist, and de-escalating may not be feasible due to fixed-dose prefilled pen preparations.

GLP-1 receptor agonists may need to be interrupted in patients who have recently started these medications or are in dose escalation phases, and have significant symptoms of fullness, nausea, and vomiting. Stopping the drugs or de-escalating doses, when possible, may be beneficial to decrease risks of aspiration in these patients who have not reached a steady state or developed tachyphylaxis to the gastrointestinal side effects. These patients may be referred to their prescribing physician for diet and medication modification before proceeding with elective procedures requiring anesthesia.

However, the first and most important intervention appears to be changing the duration of fasting for solids and possibly for liquids. Prolonged fasting time for solid foods beyond current recommendations is likely more effective than drug interruption to prevent patients from presenting on the day of procedures with residual gastric contents.[53] Data from the "real world" and gastric emptying studies support recommending a clear liquid diet for 24 h before anesthesia.[53] The fasting duration for liquids is unclear at this time, but it appears that patients who have recently started a long-acting GLP-1 receptor agonist or are in the dose escalation period and those on short-acting preparations may need a more prolonged NPO time than currently recommended. The caloric content of the liquids is important, with high-caloric clear liquids likely needing a longer fasting time than the low- or noncaloric clear liquids (8 h *vs.* 4 h). While these timeframes for liquids may appear arbitrary, data suggest that complete NPO times ranging between 4 and 12 h are more likely to result in lower gastric volumes, thus balancing the risks of aspiration with enhanced recovery principles.

Patients not tolerating the GLP-1 receptor agonist should be advised to follow a bland, low-fat, and low-fiber diet and to eat small meals. Medication changes (*i.e.*, dose de-escalation) are secondarily considered. Elective surgeries should be postponed in patients with significant symptoms refractory to these interventions. Patients who are planning dose escalation should be advised not to do so in the weeks leading up to elective procedures. Collaboration with the prescribing clinicians is important when making decisions.

Proceeding with the planned anesthetic appears safe for asymptomatic patients presenting for elective procedures who are in maintenance phases, and have followed clear liquid diets for 24 h. For symptomatic patients orthose who have not been on clear liquids for 24 h, a gastric ultrasound may help guide decisions.

Since the publication of the ASA consensus-based guidance, a number of studies have been published on the gastric emptying effects of GLP-1 receptor agonists. Therefore, we propose updated recommendations for decision-making during the preoperative period and on the day of surgery (figs. 5 and 6).

## Conclusions

Data on the perioperative management of patients taking GLP-1 receptor agonists are sparse, but emerging. There is heterogenicity as to the subjects studied (healthy controls, patients with obesity or diabetes) and the tests and measurements used, which may limit the ability to extrapolate findings across populations. Perioperative clinicians need to consider indications for medication, dosing schedule, concurrent symptoms, and the logistics of access to the medications in specific doses. Dietary recommendations, anesthetic

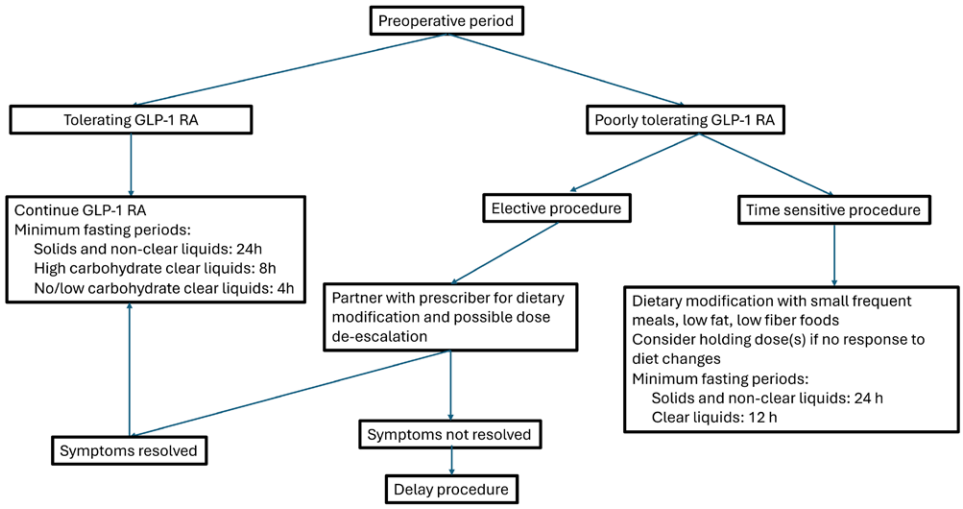


**Fig. 5.** Proposed recommendations for preoperative visit management of patients on glucagon-like peptide-1 (GLP-1) receptor agonists (RA; summary from current literature).

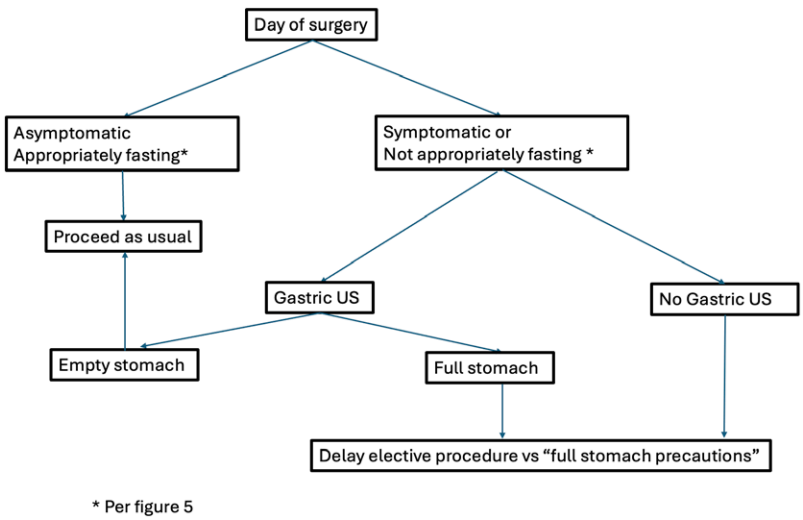


**Fig. 6.** Proposed recommendations for day of surgery management of patients on glucagon-like peptide-1 (GLP-1) receptor agonists (RA;summary from current literature). US, ultrasound.

options, and the relative urgency of the proposed procedure are also important factors to review. Indeed, a multidisciplinary, patient-centric approach is needed when caring for these patients.

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## Competing Interests

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## References

1. Nauck MA, Mirna AEA, Quast DR: Meta-analysis of head-to-head clinical trials comparing incretin-based glucose-lowering medications and basal insulin: An update including recently developed glucagon-like peptide-1 (GLP-1) receptor agonists and the glucose-dependent insulinotropic polypeptide/GLP-1 receptor co-agonist tirzepatide. Diabetes Obes Metab 2023; 25:1361–71
2. Liu L, Chen J, Wang L, Chen C, Chen L: Association between different GLP-1 receptor agonists and gastrointestinal adverse reactions: A real-world disproportionality study based on FDA adverse event reporting system database. Front Endocrinol (Lausanne) 2022; 13:1043789
3. Aldhaleei WA, Abegaz TM, Bhagavathula AS: Glucagon-like peptide-1 receptor agonists associated gastrointestinal adverse events: A cross-sectional analysis of the National Institutes of Health All of Us Cohort. Pharmaceuticals (Basel) 2024; 17:199
4. Kalas MA, Galura GM, McCallum RW: Medication-induced gastroparesis: A case report. J Investig Med High Impact Case Rep 2021; 9:23247096211051919
5. Almustanyir S, Alhabeeb H, AlHusseini N, Al Thow M: Gastroparesis with the initiation of liraglutide: A case report. Cureus 2020; 12:e11735
6. Gulak MA, Murphy P: Regurgitation under anesthesia in a fasted patient prescribed semaglutide for weight loss: A case report. Can J Anaesth 2023; 70:1397–400
7. Klein SR, Hobai IA: Semaglutide, delayed gastric emptying, and intraoperative pulmonary aspiration: A case report. Can J Anaesth 2023; 70:1394–6
8. Fujino E, Cobb KW, Schoenherr J, Gouker L, Lund E: Anesthesia considerations for a patient on semaglutide and delayed gastric emptying. Cureus 2023; 15:e42153
9. Avraham SA, Hossein J, Somri F, Hawash N, Hochman O: Pulmonary aspiration of gastric contents in two patients taking semaglutide for weight loss. Anaesth Rep 2024; 12:e12278
10. Kittner SL, Talbott AL, Vishneski SR, Narbaiza J, Shields JS: Retained gastric contents after adequate fasting associated with GLP-1 receptor agonist use: A report of 3 cases. JBJS Case Connect 2023; 13:e23.00506
11. Stark JE, Cole JL, Ghazarian RN, Klass MJ: Impact of glucagon-like peptide-1 receptor agonists (GLP-1RA) on food content during esophagogastroduodenoscopy (EGD). Ann Pharmacother 2022; 56:922–6
12. Silveira SQ, da Silva LM, de Campos Vieira Abib A, et al.: Relationship between perioperative semaglutide use and residual gastric content: A retrospective analysis of patients undergoing elective upper endoscopy. J Clin Anesth 2023; 87:111091
13. Sherwin M, Hamburger J, Katz D, DeMaria S: Influence of semaglutide use on the presence of residual gastric solids on gastric ultrasound: A prospective observational study in volunteers without obesity recently started on semaglutide. Can J Anaesth 2023; 70:1300–6
14. Kobori T, Onishi Y, Yoshida Y, et al.: Association of glucagon-like peptide-1 receptor agonist treatment with gastric residue in an esophagogastroduodenoscopy. J Diabetes Investig 2023; 14:767–73

15. Nadeem D, Taye M, Still MD, et al.: Effects of glucagon-like peptide-1 receptor agonists on upper endoscopy in diabetic and non-diabetic patients. Gastrointest Endosc 2024:S0016–5107(24)03159 [Epub ahead of print]
16. Firkins SA, Yates J, Shukla N, Garg R, Vargo JJ, Lembo A; Cleveland Clinic Obesity Medicine and Bariatric Endoscopy Working Group: Clinical outcomes and safety of upper endoscopy while on glucagon-like peptide-1 receptor agonists. Clin Gastroenterol Hepatol 2024:S1542–3565(24)00295 [Epub ahead of print]
17. Garza K, Aminpour E, Shah J, et al.: Glucagon-like peptide-1 receptor agonists increase solid gastric residue rates on upper endoscopy especially in patients with complicated diabetes: A case-control study. Am J Gastroenterol 2024; 119:1081–8
18. Wu F, Smith MR, Mueller AL, et al.: Association of glucagon-like peptide receptor 1 agonist therapy with the presence of gastric contents in fasting patients undergoing endoscopy under anesthesia care: A historical cohort study. Can J Anaesth 2024; 71:958–66
19. Anazco D, Fansa S, Hurtado MD, Camilleri M, Acosta A: Low incidence of pulmonary aspiration during upper endoscopy in patients prescribed a glucagon-like peptide 1 receptor agonist. Clin Gastroenterol Hepatol 2024; 22:1333–5.e2
20. Dixit AA, Bateman BT, Hawn MT, Odden MC, Sun EC: Preoperative GLP-1 receptor agonist use and risk of postoperative respiratory complications. JAMA 2024; 331:1672–3
21. Sen S, Potnuru PP, Hernandez N, et al.: Glucagon-like peptide-1 receptor agonist use and residual gastric content before anesthesia. JAMA Surg 2024; 159:660–7
22. Joshi GP, Abdelmalak BB, Weigel WA, et al: American Society of Anesthesiologists consensus-based guidance on preoperative management of patients (adults and children) on glucagon-like peptide-1 (GLP-1) receptor agonists. June 29, 2023. Available at: https://www.asahq.org/about-asa/newsroom/news-releases/2023/06/american-society-of-anesthesiologists-consensus-based-guidance-on-preoperative. Accessed May 27, 2024.
23. Knop FK, Brønden A, Vilsbøll T: Exenatide: Pharmacokinetics, clinical use, and future directions. Expert Opin Pharmacother 2017; 18:555–71
24. Jacobsen LV, Flint A, Olsen AK, Ingwersen SH: Liraglutide in type 2 diabetes mellitus: Clinical pharmacokinetics and pharmacodynamics. Clin Pharmacokinet 2016; 55:657–72
25. Geiser JS, Heathman MA, Cui X, et al.: Clinical pharmacokinetics of dulaglutide in patients with type 2 diabetes: Analyses of data from clinical trials. Clin Pharmacokinet 2016; 55:625–34
26. Nauck MA, Quast DR, Wefers J, Meier JJ: GLP-1 receptor agonists in the treatment of type 2 diabetes - State-of-the-art. Mol Metab 2021; 46:101102
27. Rosenstock J, Frias J, Jastreboff AM, et al.: Retatrutide, a GIP, GLP-1 and glucagon receptor agonist, for people with type 2 diabetes: A randomised, double-blind, placebo and active-controlled, parallel-group, phase 2 trial conducted in the USA. Lancet 2023; 402:529–44
28. Wharton S, Blevins T, Connery L, et al.; GZGI Investigators: Daily oral GLP-1 receptor agonist orforglipron for adults with obesity. N Engl J Med 2023; 389:877–88
29. Jastreboff AM, Kaplan LM, Frías JP, et al.; Retatrutide Phase 2 Obesity Trial Investigators: Triple-hormone-receptor agonist retatrutide for obesity - A phase 2 trial. N Engl J Med 2023; 389:514–26
30. Lee YS, Jun HS: Anti-diabetic actions of glucagon-like peptide-1 on pancreatic beta-cells. Metabolism 2014; 63:9–19
31. Nauck MA, Meier JJ: Management of endocrine disease: Are all GLP-1 agonists equal in the treatment of type 2 diabetes? Eur J Endocrinol 2019; 181:R211–34
32. Zhao X, Wang M, Wen Z, et al.: GLP-1 receptor agonists: Beyond their pancreatic Effects. Front Endocrinol (Lausanne) 2021; 12:721135
33. Stefanou MI, Theodorou A, Malhotra K, et al.: Risk of major adverse cardiovascular events and stroke associated with treatment with GLP-1 or the dual GIP/GLP-1 receptor agonist tirzepatide for type 2 diabetes: A systematic review and meta-analysis. Eur Stroke J 2024; 9:530–9
34. Singh S, Garg A, Tantry US, Bliden K, Gurbel PA, Gulati M: Safety and efficacy of glucagon-like peptide-1 receptor agonists on cardiovascular events in overweight or obese non-diabetic patients. Curr Probl Cardiol 2024; 49:102403
35. American Diabetes Association Professional Practice Committee: 9. Pharmacologic approaches to glycemic treatment: Standards of care in diabetes-2024. Diabetes Care 2024; 47:S158–78
36. Samson SL, Vellanki P, Blonde L, et al.: American Association of Clinical Endocrinology consensus statement: Comprehensive type 2 diabetes management algorithm - 2023 Update. Endocr Pract 2023; 29:305–40
37. Polderman JAW, van Steen SCJ, Thiel BG, et al.: Perioperative management of patients with type-2 diabetes mellitus undergoing non-cardiac surgery using liraglutide, glucose-insulin-potassium infusion or intravenous insulin bolus regimens: A randomised controlled trial. Anaesthesia 2018; 73:332–9
38. Hulst AH, Visscher MJ, Godfried MB, et al.; GLOBE Study Group: Liraglutide for perioperative management of hyperglycaemia in cardiac surgery patients: A multicentre randomized superiority trial. Diabetes Obes Metab 2020; 22:557–65
39. Makino H, Tanaka A, Asakura K, et al.: Addition of low-dose liraglutide to insulin therapy is useful for glycaemic control during the peri-operative period: Effect of glucagon-like peptide-1 receptor agonist therapy on

glycaemic control in patients undergoing cardiac surgery (GLOLIA study). Diabet Med 2019; 36:1621–8
40. Lipš M, Mráz M, Kloučková J, et al.: Effect of continuous exenatide infusion on cardiac function and peri-operative glucose control in patients undergoing cardiac surgery: A single-blind, randomized controlled trial. Diabetes Obes Metab 2017; 19:1818–22
41. Besch G, Perrotti A, Mauny F, et al.: Clinical effectiveness of intravenous exenatide infusion in perioperative glycemic control after coronary artery bypass graft surgery: A phase II/III randomized trial. Anesthesiology 2017; 127:775–87
42. Watkins AR, Fialka N, El-Andari R, Kang JJ, Bozso SJ, Nagendran J: Effect of glucagon-like peptide-1 receptor agonists administration during coronary artery bypass grafting: A systematic review and meta-analysis of randomized control trials. Future Cardiol 2023; 19:105–15
43. Kaneko S, Ueda Y, Tahara Y: GLP1 receptor agonist liraglutide is an effective therapeutic option for perioperative glycemic control in type 2 diabetes within Enhanced Recovery After Surgery (ERAS) protocols. Eur Surg Res 2018; 59:349–60
44. Magruder ML, Miskiewicz MJ, Rodriguez AN, Mont MA: Semaglutide use prior to total hip arthroplasty results in fewer postoperative prosthetic joint infections and readmissions. J Arthroplasty 2024; 39:716–20
45. Jalleh RJ, Jones KL, Rayner CK, Marathe CS, Wu T, Horowitz M: Normal and disordered gastric emptying in diabetes: Recent insights into (patho)physiology, management and impact on glycaemic control. Diabetologia 2022; 65:1981–93
46. Weber M, Siddarthan I, Mack PF: Clinically significant emesis in a patient taking a long-acting GLP-1 receptor agonist for weight loss. Br J Anaesth 2023; 131:e37–9
47. Yeo YH, Gaddam S, Ng WH, Huang P-C, Ma KS, Rezaie A; Motility and Metabolic Pharmacoepidemiology Group: Increased risk of aspiration pneumonia associated with endoscopic procedures among patients with glucagon-like peptide 1 receptor agonist use. Gastroenterology 2024; 167:402–4.e3
48. Klonoff DC, Kim SH, Galindo RJ, et al.: Risks of peri- and postoperative complications with glucagon-like peptide-1 receptor agonists. Diabetes Obes Metab 2024; 26:3128–36.
49. Barlowe TS, Anderson C, Sandler RS, et al.: Glucagon-like peptide-1 receptor agonists do not increase aspiration during upper endoscopy in patients with diabetes. Clin Gastroenterol Hepatol 2024:S1542–3565(24)00453 [Epub ahead of print]
50. Queiroz VNF, Falsarella PM, Chaves RCF, Takaoka F, Socolowski LR, Garcia RG: Risk of pulmonary aspiration during semaglutide use and anesthesia in a fasting patient: A case report with tomographic evidence. Einstein (Sao Paulo) 2023; 21:eRC0628
51. Hodgson JA, Rivera-Rodriguez H, Wu P, Udani J, Weiss J: Point-of-care ultrasound aids in the management of patient taking semaglutide before surgery: A case report. A A Pract 2024; 18:e01762
52. Chapman MB, Norwood DA, Price C, et al.: Effects of glucagon-like peptide-1 receptor agonists on gastric mucosal visibility and retained gastric contents during esophagogastroduodenoscopy. Gastrointest Endosc 2024:S0016–5107(24)03208 [Epub ahead of print]
53. Maselli DB, Lee D, Bi D, et al.: Safe continuation of glucagon-like peptide 1 receptor agonists at endoscopy: A case series of 57 adults undergoing endoscopic sleeve gastroplasty. Obes Surg 2024; 34:2369–74
54. Acosta A, Camilleri M, Burton D, et al.: Exenatide in obesity with accelerated gastric emptying: A randomized, pharmacodynamics study. Physiol Rep 2015; 3:e12610
55. Linnebjerg H, Park S, Kothare PA, et al.: Effect of exenatide on gastric emptying and relationship to postprandial glycemia in type 2 diabetes. Regul Pept 2008; 151:123–9
56. Kuwata H, Yabe D, Murotani K, et al.: Effects of glucagon-like peptide-1 receptor agonists on secretions of insulin and glucagon and gastric emptying in Japanese individuals with type 2 diabetes: A prospective, observational study. J Diabetes Investig 2021; 12:2162–71
57. Quast DR, Schenker N, Menge BA, Nauck MA, Kapitza C, Meier JJ: Effects of lixisenatide versus liraglutide (short- and long-acting GLP-1 receptor agonists) on esophageal and gastric function in patients with type 2 diabetes. Diabetes Care 2020; 43:2137–45
58. Lorenz M, Pfeiffer C, Steinsträsser A, et al.: Effects of lixisenatide once daily on gastric emptying in type 2 diabetes--Relationship to postprandial glycemia. Regul Pept 2013; 185:1–8
59. Meier JJ, Menge BA, Schenker N, et al.: Effects of sequential treatment with lixisenatide, insulin glargine, or their combination on meal-related glycaemic excursions, insulin and glucagon secretion, and gastric emptying in patients with type 2 diabetes. Diabetes Obes Metab 2020; 22:599–611
60. Meier JJ, Rosenstock J, Hincelin-Méry A, et al.: Contrasting effects of lixisenatide and liraglutide on postprandial glycemic control, gastric emptying, and safety parameters in patients with type 2 diabetes on optimized insulin glargine with or without metformin: A randomized, open-label trial. Diabetes Care 2015; 38:1263–73
61. Jones KL, Huynh LQ, Hatzinikolas S, et al.: Exenatide once weekly slows gastric emptying of solids and liquids in healthy, overweight people at steady-state concentrations. Diabetes Obes Metab 2020; 22:788–97
62. Maselli D, Atieh J, Clark MM, et al.: Effects of liraglutide on gastrointestinal functions and weight in obesity: A randomized clinical and pharmacogenomic trial. Obesity (Silver Spring) 2022; 30:1608–20

63. Nagai Y, Hashimoto E, Oikawa R, et al.: Differing effects of liraglutide on gastric emptying in Japanese patients with type 2 diabetes. Diabetes Obes Metab 2014; 16:573–6
64. Halawi H, Khemani D, Eckert D, et al.: Effects of liraglutide on weight, satiation, and gastric functions in obesity: A randomised, placebo-controlled pilot trial. Lancet Gastroenterol Hepatol 2017; 2:890–9
65. Nakatani Y, Maeda M, Matsumura M, et al.: Effect of GLP-1 receptor agonist on gastrointestinal tract motility and residue rates as evaluated by capsule endoscopy. Diabetes Metab 2017; 43:430–7
66. Jensterle M, Ferjan S, Ležaič L, et al.: Semaglutide delays 4-hour gastric emptying in women with polycystic ovary syndrome and obesity. Diabetes Obes Metab 2023; 25:975–84
67. Cervera A, Wajcberg E, Sriwijitkamol A, et al.: Mechanism of action of exenatide to reduce postprandial hyperglycemia in type 2 diabetes. Am J Physiol Endocrinol Metab 2008; 294:E846–52
68. DeFronzo RA, Okerson T, Viswanathan P, Guan X, Holcombe JH, MacConell L: Effects of exenatide versus sitagliptin on postprandial glucose, insulin and glucagon secretion, gastric emptying, and caloric intake: A randomized, cross-over study. Curr Med Res Opin 2008; 24:2943–52
69. Drucker DJ, Buse JB, Taylor K, et al.; DURATION-1 Study Group: Exenatide once weekly versus twice daily for the treatment of type 2 diabetes: A randomised, open-label, non-inferiority study. Lancet 2008; 372:1240–50
70. Kolterman OG, Kim DD, Shen L, et al.: Pharmacokinetics, pharmacodynamics, and safety of exenatide in patients with type 2 diabetes mellitus. Am J Health Syst Pharm 2005; 62:173–81
71. Juel CTB, Lund A, Andersen MM, et al.: The GLP-1 receptor agonist lixisenatide reduces postprandial glucose in patients with diabetes secondary to total pancreatectomy: A randomised, placebo-controlled, double-blinded crossover trial. Diabetologia 2020; 63:1285–98
72. Becker RH, Stechl J, Steinstraesser A, Golor G, Pellissier F: Lixisenatide reduces postprandial hyperglycaemia via gastrostatic and insulinotropic effects. Diabetes Metab Res Rev 2015; 31:610–8
73. Jones KL, Rigda RS, Buttfield MDM, et al.: Effects of lixisenatide on postprandial blood pressure, gastric emptying and glycaemia in healthy people and people with type 2 diabetes. Diabetes Obes Metab 2019; 21:1158–67
74. Jalleh R, Pham H, Marathe CS, et al.: Acute effects of lixisenatide on energy intake in healthy subjects and patients with type 2 diabetes: Relationship to gastric emptying and intragastric distribution. Nutrients 2020; 12:1962
75. Rayner CK, Watson LE, Phillips LK, et al.: Effects of sustained treatment with lixisenatide on gastric emptying and postprandial glucose metabolism in type 2 diabetes: A randomized controlled trial. Diabetes Care 2020; 43:1813–21
76. Kovoor JG, Rayner CK, Wu T, et al.: Effect of lixisenatide on liquid gastric emptying in type 2 diabetes - Implications for the use of GLP-1 receptor agonists before procedures. J Diabetes Complications 2024; 38:108793
77. Barrington P, Chien JY, Showalter HD, et al.: A 5-week study of the pharmacokinetics and pharmacodynamics of LY2189265, a novel, long-acting glucagon-like peptide-1 analogue, in patients with type 2 diabetes. Diabetes Obes Metab 2011; 13:426–33
78. Degn KB, Juhl CB, Sturis J, et al.: One week's treatment with the long-acting glucagon-like peptide 1 derivative liraglutide (NN2211) markedly improves 24-h glycemia and alpha- and beta-cell function and reduces endogenous glucose release in patients with type 2 diabetes. Diabetes 2004; 53:1187–94
79. Dejgaard TF, Frandsen CS, Hansen TS, et al.: Efficacy and safety of liraglutide for overweight adult patients with type 1 diabetes and insufficient glycaemic control (Lira-1): A randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol 2016; 4:221–32
80. Flint A, Kapitza C, Hindsberger C, Zdravkovic M: The once-daily human glucagon-like peptide-1 (GLP-1) analog liraglutide improves postprandial glucose levels in type 2 diabetes patients. Adv Ther 2011; 28:213–26
81. Horowitz M, Flint A, Jones KL, et al.: Effect of the once-daily human GLP-1 analogue liraglutide on appetite, energy intake, energy expenditure and gastric emptying in type 2 diabetes. Diabetes Res Clin Pract 2012; 97:258–66
82. van Can J, Sloth B, Jensen CB, Flint A, Blaak EE, Saris WH: Effects of the once-daily GLP-1 analog liraglutide on gastric emptying, glycemic parameters, appetite and energy metabolism in obese, non-diabetic adults. Int J Obes (Lond) 2014; 38:784–93
83. Saxena AR, Banerjee A, Corbin KD, Parsons SA, Smith SR: Energy intake as a short-term biomarker for weight loss in adults with obesity receiving liraglutide: A randomized trial. Obes Sci Pract 2021; 7:281–90
84. Hjerpsted JB, Flint A, Brooks A, Axelsen MB, Kvist T, Blundell J: Semaglutide improves postprandial glucose and lipid metabolism, and delays first-hour gastric emptying in subjects with obesity. Diabetes Obes Metab 2018; 20:610–9
85. Dahl K, Brooks A, Almazedi F, Hoff ST, Boschini C, Baekdal TA: Oral semaglutide improves postprandial glucose and lipid metabolism, and delays gastric emptying, in subjects with type 2 diabetes. Diabetes Obes Metab 2021; 23:1594–603
86. Friedrichsen M, Breitschaft A, Tadayon S, Wizert A, Skovgaard D: The effect of semaglutide 2.4 mg once

weekly on energy intake, appetite, control of eating, and gastric emptying in adults with obesity. Diabetes Obes Metab 2021; 23:754–62
87. Urva S, Coskun T, Loghin C, et al.: The novel dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 (GLP-1) receptor agonist tirzepatide transiently delays gastric emptying similarly to selective long-acting GLP-1 receptor agonists. Diabetes Obes Metab 2020; 22:1886–91
88. Maselli DB, Camilleri M: Effects of GLP-1 and its analogs on gastric physiology in diabetes mellitus and obesity. Adv Exp Med Biol 2021; 1307:171–92
89. Joshi GP, Abdelmalak BB, Weigel WA, et al.: 2023 American Society of Anesthesiologists practice guidelines for preoperative fasting: Carbohydrate-containing clear liquids with or without protein, chewing gum, and pediatric fasting duration-A modular update of the 2017 American Society of Anesthesiologists Practice Guidelines for Preoperative Fasting. Anesthesiology 2023; 138:132–51
90. Hiramoto B, McCarty TR, Lodhia NA, et al.: Quantified metrics of gastric emptying delay by GLP-1 agonists: A systematic review and meta-analysis with insights for periprocedural management. Am J Gastroenterol 2024; 119:1126–40
91. Carlsson Petri KC, Ingwersen SH, Flint A, Zacho J, Overgaard RV: Semaglutide s.c. once-weekly in type 2 diabetes: A population pharmacokinetic analysis. Diabetes Ther 2018; 9:1533–47
92. Schneck K, Urva S: Population pharmacokinetics of the GIP/GLP receptor agonist tirzepatide. CPT Pharmacometrics Syst Pharmacol 2024; 13:494–503
93. Whitley HP, Trujillo JM, Neumiller JJ: Special report: Potential strategies for addressing GLP-1 and dual GLP-1/GIP receptor agonist shortages. Clin Diabetes 2023; 41:467–73
94. Arunachala Murthy T, Chapman M, Jones KL, Horowitz M, Marathe CS: Inter-relationships between gastric emptying and glycaemia: Implications for clinical practice. World J Diabetes 2023; 14:447–59
95. Gorgojo-Martínez JJ, Mezquita-Raya P, Carretero-Gómez J, et al.: Clinical recommendations to manage gastrointestinal adverse events in patients treated with Glp-1 receptor agonists: A multidisciplinary expert consensus. J Clin Med 2022; 12:145
96. Wharton S, Davies M, Dicker D, et al.: Managing the gastrointestinal side effects of GLP-1 receptor agonists in obesity: Recommendations for clinical practice. Postgrad Med 2022; 134:14–9
97. Yao R, Gala KS, Ghusn W, Abboud DM, Wallace FK, Vargas EJ: Effect of glucagon-like peptide-1 receptor agonists on bowel preparation for colonoscopy. Am J Gastroenterol 2024; 119:1154–7
98. Rüggeberg A, Meybohm P, Nickel EA: Preoperative fasting and the risk of pulmonary aspiration-a narrative review of historical concepts, physiological effects, and new perspectives. BJA Open 2024; 10:100282
99. Korytkowski MT, Muniyappa R, Antinori-Lent K, et al.: Management of hyperglycemia in hospitalized adult patients in non-critical care settings: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2022; 107:2101–28
100. Girón-Arango L, Perlas A: Point-of-care gastric ultrasound to identify a full stomach on a diabetic patient taking a glucagon-like peptide 1 receptor agonist. A A Pract 2024; 18:e01751
101. Willson CM, Patel L, Middleton P, Desai M: Glucagon-like peptide-1 agonists and general anesthesia: Perioperative considerations and the utility of gastric ultrasound. Cureus 2024; 16:e58042