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Q: Should glucagon-like peptide 1 receptor agonists be withheld during the preoperative period?

A 58-year-old man with type 2 diabetes, a body mass index of 35 kg/m², and a history of recurrent right upper quadrant pain due to cholelithiasis is scheduled for elective laparoscopic cholecystectomy. His diabetes is well controlled with a glucagon-like peptide (GLP) 1 receptor agonist. Should GLP-1 receptor agonist therapy be withheld before the procedure? If so, when should it be discontinued?

A: Clinical judgment should guide decisions on whether to withhold GLP-1 receptor agonists before elective surgical procedures, taking into account patient symptoms, the presence of factors that increase risk for aspiration such as dysmotility disorders, and the clinical situation.

When discontinuing therapy, current clinical practice guidance from the American Society of Anesthesiologists recommends that GLP-1 receptor agonists be preoperatively withheld according to their dosing schedules, with daily administered agents withheld the day of the procedure and weekly administered agents withheld for 1 week before the procedure.¹

■ WHY CONSIDER HOLDING GLP-1 RECEPTOR AGONISTS BEFORE SURGICAL PROCEDURES?

GLP-1 receptor agonists recapitulate the activity of the gut-derived hormone incretin, which is secreted at the time of food ingestion to help regulate blood glucose levels and satiety. GLP-1 receptor agonists delay gastric emptying, leading to concerns about retention of gastric contents even in patients who have followed fasting guidelines.² In addition, nausea and vomiting are common gastrointestinal side effects of GLP-1 receptor inhibitors, especially during the initiation

phase of therapy or when they are taken at high doses. As such, patients taking GLP-1 receptor agonists may have an increased risk of aspiration of gastric contents during sedation and anesthesia.

The GLP-1 receptor agonists currently available in the United States have varying half-lives and observed delays in gastric emptying (Table 1).² GLP-1 receptor agonists with half-lives ranging from 5 to 7 days generally delay gastric emptying by 1 to 2 hours, whereas GLP-1 receptor agonists with half-lives ranging from 2 to 13 hours delay gastric emptying by 1 to 3 hours.

In a systematic review by Hiramoto et al,³ solid-phase gastric emptying for patients taking GLP-1 receptor agonists was delayed by approximately 36 minutes (72% retention at 2 hours and 37% at 4 hours), although the clinical importance of this is unclear. Liquid-phase emptying was minimally affected, with no difference in acetaminophen absorption time between GLP-1 receptor agonist and placebo. These findings indicate a notable but not severe delay in solid-phase emptying, with liquid-phase emptying normalizing within 4 to 5 hours after ingestion.

■ WHAT FACTORS SHOULD INFORM THE DECISION TO HOLD GLP-1 RECEPTOR AGONISTS BEFORE AN ELECTIVE SURGICAL PROCEDURE?

Shared decision-making

The care team (surgical, anesthesiology, and prescribing clinicians) should use clinical judgment and evaluate the risks of GLP-1 receptor agonist administration well before a surgical procedure to allow time for adjustments. Such adjustments may include dietary changes or use of bridging medications if GLP-1 receptor agonist discontinuation is needed, although

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TABLE 1
Glucagon-like peptide 1 receptor agonists approved in the United States

Generic name	Administration route and frequency	Half-life	Gastric emptying delay
Dulaglutide	Subcutaneous injection weekly	5 days	120 minutes
Exenatide	Subcutaneous injection twice daily	2–3 hours	100–120 minutes
Exenatide, extended release	Subcutaneous injection weekly	8–14 days	144 minutes
Liraglutide	Subcutaneous injection daily	11–15 hours	70 minutes (median)
Semaglutide injection	Subcutaneous injection weekly	1 week	60 minutes
Semaglutide tablets	Oral daily	1 week	Unknown

Based on information from reference 2.

bridging may be resource intensive and increase risks such as hypoglycemia.⁴

Risks of discontinuing vs continuing

The decision to withhold GLP-1 receptor agonists before a procedure ultimately depends on the risk of aspiration vs the need for metabolic stability. Recent multisociety clinical practice guidance lists several factors that are considered to increase risk for delayed gastric emptying and aspiration perioperatively in patients taking GLP-1 receptor agonists⁴:

- Being in the dose-escalation phase of GLP-1 receptor agonist treatment
- Taking higher doses or weekly doses
- Having gastrointestinal symptoms of delayed gastric emptying (eg, nausea, vomiting, constipation)
- Having conditions that may delay gastric emptying, including gastroparesis and Parkinson disease.

The guidance notes that patients without these risk factors may continue GLP-1 receptor agonists before a surgical procedure.

The primary indication for GLP-1 receptor agonist therapy also may inform the decision of whether to withhold it preoperatively. For patients with obesity, in whom the risk of bronchoaspiration is higher, preoperative interruption of GLP-1 receptor agonist therapy

may reduce residual gastric content and aspiration risk.² Note, however, that withholding of GLP-1 receptor agonists solely due to the presence of overweight or obesity, without a specific risk factor outlined above, may lead to bias against patients with these conditions.⁴ For patients with type 2 diabetes, this decision should be individualized because of the risk of perioperative hyperglycemia and its association with poor outcomes.

Notably, discontinuing GLP-1 receptor agonists for patients with type 2 diabetes and cardiovascular disease may increase the risk of cardiac decompensation, worsening blood pressure and fluid retention and thereby exacerbating heart failure symptoms.⁵ Reduced glycemic control and potential weight gain may also increase cardiac stress, while increased sympathetic activity and vascular stiffness may raise afterload, further straining the heart.

WHAT ARE RECOMMENDATIONS FOR HOLDING GLP-1 RECEPTOR AGONISTS BEFORE AN ELECTIVE SURGICAL PROCEDURE?

Guidance on duration of interruption

No evidence-based guidelines are currently available regarding how long GLP-1 receptor agonists should be interrupted during the preoperative period.^{4,6} According to the American Society of Anesthesiologists consensus-based guidance on preoperative management of patients,¹ GLP-1 receptor agonists with daily dosing regimens should be withheld on the day of the procedure. GLP-1 receptor agonists with weekly dosing regimens should be withheld 1 week before the procedure. These recommendations apply regardless of the indication for GLP-1 receptor agonist use (ie, diabetes or weight loss), dose of GLP-1 receptor agonist, or procedure type.

Day-of-procedure guidance

If the patient has gastrointestinal tract symptoms (ie, nausea, vomiting, abdominal pain, or constipation) at the time of the procedure, the procedure should be delayed and the risk of aspiration discussed.¹ If the patient does not have gastrointestinal tract symptoms at the time of the procedure and has withheld GLP-1 receptor agonists for the recommended time, the procedure may be performed as planned. If the patient does not have gastrointestinal tract symptoms but has not withheld GLP-1 receptor agonist treatment according to recommendations, the procedure may be performed with *full stomach precautions*. These precautions include ensuring appropriate fasting (ie, 6 hours for solids and 2 hours for clear liquids), using rapid-sequence induction with cricoid pressure, administering antacids or

prokinetics, avoiding positive pressure ventilation, elevating the head, and delaying extubation until the patient is fully awake and can protect their airway.

If aspiration risk is a concern, point-of-care gastric ultrasonography should be used to assess stomach contents.⁴ If the stomach is empty, the procedure may proceed as planned. For patients with confirmed gastric retention or a high risk of aspiration, rapid sequence induction and intubation should be considered to reduce aspiration risk and avoid canceling the procedure. American Society of Anesthesiologists practice guidelines⁷ on fasting should be followed in all cases because of a lack of specific evidence for GLP-1 receptor agonist use.

GLP-1 receptor agonists may be restarted after the procedure is completed, although the optimal timing for restarting them is currently unclear and would vary based on the type of procedure performed.

■ WHAT ARE RECOMMENDATIONS FOR HOLDING GLP-1 RECEPTOR AGONISTS BEFORE AN ENDOSCOPIC PROCEDURE?

According to American Gastroenterological Association rapid clinical practice update on the management of patients taking GLP-1 receptor agonists prior to endoscopy,⁸ GLP-1 receptor agonist use for diabetes management should be continued before endoscopy to maintain glycemic control. Gastrointestinal tract symptoms should be closely monitored. If no symptoms are apparent and fasting protocols are followed, the procedure may be performed as planned. For patients using GLP-1 receptor agonists for weight loss, withholding a dose before an endoscopic procedure should be considered, although this is not mandatory or evidence based.

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If nausea or gastric retention is present the day of the procedure, further evaluation or management of these symptoms may be needed. For patients with serious gastrointestinal tract symptoms, transabdominal ultrasonography should be considered to assess gastric contents and determine whether the procedure should be delayed. Consuming a liquid diet the day before the procedure may be a safer alternative to stopping GLP-1 receptor agonist therapy.⁸

■ THE BOTTOM LINE

Patients at increased risk of aspiration who will undergo deep sedation or general anesthesia (especially those starting GLP-1 receptor agonist therapy or taking a high dose) may benefit from withholding GLP-1 receptor agonists.⁴ For those who do not have an elevated risk of delayed gastric emptying and aspiration and are undergoing procedures with low aspiration risk (moderate sedation or local anesthesia), GLP-1 receptor agonist continuation may be safe. Strategies that may mitigate aspiration risks and allow continuation of GLP-1 receptor agonist therapy include a 24-hour preoperative clear liquid diet, rapid-sequence induction, or gastric ultrasonography to assess for retained gastric contents.

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■ DISCLOSURES

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