CLINICAL PRACTICE UPDATES

AGA Rapid Clinical Practice Update on the Management of Patients Taking GLP-1 Receptor Agonists Prior to Endoscopy: Communication

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DESCRIPTION: **The purpose of this American Gastroenterological Association (AGA) Institute Rapid Clinical Practice Update (CPU) Communication is to review the available evidence and provide expert advice regarding the evolving management of patients taking GLP-1 receptor agonists prior to endoscopy.**

METHODS: **This CPU was commissioned and approved by the AGA Institute Clinical Practice Updates Committee (CPUC) and the AGA Governing Board to provide timely guidance on a topic of high clinical importance to the AGA membership and underwent internal peer review by the CPUC and external peer review through standard procedures of Clinical Gastroenterology and Hepatology. This communication incorporates important and recently published studies in this field, and it reflects the experiences of the authors who are experts in bariatric medicine and/or endoscopy.**

Keywords: Glucagon-like peptide; Anesthesia; Sedation; Semaglutide; Ozempic; Wegovy.

Clinical Dilemma

There has been increasing concern about performing endoscopic procedures, in particular upper endoscopies, on patients who are using glucagon-like peptide 1 (GLP-1) receptor agonists (GLP-1 RAs) because of their effect on slowing gastric motility and the risk of aspiration of retained gastric contents in sedated patients. Although data are quite limited, the American Society of Anesthesiologists (ASA) recently released the following consensus-based perioperative guidance:[1] "For patients on daily dosing consider holding GLP-1 agonists on the day of the procedure/surgery. For patients on weekly dosing consider holding GLP-1 agonists a week prior to the procedure/surgery. This suggestion is irrespective of the indication (type 2 diabetes mellitus or weight loss), dose, or the type of procedure/surgery. If the patient has no GI symptoms, but the GLP-1 agonists were not held as advised, proceed with 'full stomach' precautions…"

As a result, anesthesia providers have begun canceling or postponing endoscopic procedures in patients taking this class of medication who require sedation or proceeding to general endotracheal intubation in some situations, which may lead to added time, cost, and clinical risk to patients. Many facilities and medical centers are now struggling to revise preprocedural protocols for patients taking this class of medications despite the lack of high-level evidence regarding how to proceed.

The objective of this AGA Rapid Clinical Practice Update is to address concerns voiced by gastroenterologists, endoscopists, patients, practices, and health systems about this clinical dilemma. Important questions include whether these preprocedural changes are necessary, if they truly mitigate periprocedural aspiration, or if the delays instituted by following this guidance might further compound the major problem currently faced nationwide: that of large numbers of patients awaiting endoscopic procedures because of delays from the COVID-19 pandemic, reduction in the recommended age threshold to start colorectal cancer screening in 2018, and workforce challenges.[2–4] It is clear that well-designed studies investigating patients on GLP-1 RAs who require endoscopy are needed.

Abbreviations used in this paper: **ASA, American Society of Anesthesiologists; GLP-1, glucagon-like peptide 1; RA, receptor agonist.**

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Background

The use of GLP-1 RAs has dramatically increased since being approved in 2005 for the treatment of type 2 diabetes mellitus. More recently, this class of medication has been approved for weight loss with data showing that patients may lose up to 20% of their weight,[5,6] which may help address the obesity epidemic, a major public health concern in the United States and worldwide.[7] Importantly, GLP-1 RAs have also been associated with improvement in metabolic syndrome and cardiac risk, even in patients without diabetes.[6,8]

GLP-1 RAs (eg, semaglutide, tirzepatide, exenatide, liraglutide, albiglutide, dulaglutide, and lixisneatide) mimic incretins, which are hormones released after eating that prompt glucose-dependent insulin release from the pancreatic islets, stimulate satiety centers, inhibit glucagon release, and result in diminished gastric emptying.[9] Patients receiving GLP-1 RAs may have gastrointestinal side effects including nausea, vomiting, diarrhea, or constipation.[9] GLP-1 RAs have been associated with increased gastric residue in patients with diabetes undergoing upper endoscopy.[10] There also have been published case reports showing that GLP-1 RA use was associated with increased gastric retention of solids rather than liquids.[11,12] Patients receiving GLP-1 RAs who experienced nausea, vomiting, dyspepsia, or abdominal bloating were found to have higher residual gastric contents.[12] In a recent prospective observational study, transabdominal gastric ultrasound to assess for solid-food residue was performed on patients receiving GLP-1 RAs, and compared with control subjects, after having fasted for at least 10 hours.[13] Patients taking GLP-1 RAs had delayed gastric emptying and increased residual gastric contents after an overnight fast.[13] These findings imply an increased risk of aspiration in patients receiving GLP-1 RA medications who present for procedures that require sedation.[14]

It is important to understand that rates of solid and liquid gastric emptying differ. The normal stomach secretes up to 2–3 L of fluid/day, which readily passes.[15] $T_{1/2}$ for liquid gastric emptying is estimated at 23 minutes, whereas abnormal solid-food gastric emptying is described as >60% retention at 2 hours and >10% retention at 4 hours on scintigraphy studies. Fluid is less of an issue because it is easily removed during an esophagogastroduodenoscopy, and this is the first maneuver performed by endoscopists on entering the stomach. In fact, in a study comparing patients taking semaglutide with control subjects, although there was an increased risk of residual gastric contents in the semaglutide group, a protective effect (0.25; 95% confidence interval, 0.16–0.39) against retained gastric contents was found in patients undergoing esophagogastroduodenoscopy and colonoscopy (but not esophagogastroduodenoscopy alone), presumably because of fasting and consumption of only a liquid diet the day before.[12]

Patients with gastroparesis from various causes, including those taking other medications, such as opioids,[16] may also be at an increased risk for aspiration during sedated endoscopies. However, no special dietary precautions or medication adjustments are routinely prescribed for these patients before upper endoscopy with deep sedation provided by an anesthesia professional or moderate sedation administered by a nurse and gastrointestinal endoscopist. In patients with severe gastroparesis who are scheduled to undergo gastric peroral endoscopic myotomy (where a stomach devoid of food is critical) it is advised that patients stop ingesting solid foods and be maintained on clear liquids only the day before their procedure.[17]

Clinical Strategies

It is appropriate that the ASA's perioperative suggestions for patients on GLP-1 RAs are labeled "consensus-based guidance on perioperative management," because there is clearly insufficient published evidence for a robust systematic review and guideline. The ASA used such terms as "suggest," "consider," and "advise," as we would in an AGA Clinical Practice Update. Were a rigorous guideline produced using GRADE methodology, there would be insufficient evidence to support recommendations derived from corresponding PICOs. As such, the ASA's suggestions are expert opinions, which may inform but should not replace clinical judgment. Overemphasis or widespread implementation of expert opinion may be associated with unintended harms. These were among the reasons for release of a multisociety statement entitled, "No data to support stopping GLP-1 agonists prior to elective endoscopy."[18]

We suggest that an individualized approach be taken to managing patients on GLP-1 RAs in the pre-endoscopic setting. The clinical team should be cognizant of the indication for the GLP-1 RAs, because cessation in patients relying on this medication for diabetes management might provide more risk than benefit. Additionally, the dose and frequency, other comorbidities and medications, and most importantly gastrointestinal symptoms/side effects commonly experienced from these drugs (eg, nausea, vomiting, dyspepsia, and early satiety) should be noted. If patients taking GLP-1 RAs solely for weight loss can be identified beforehand, a dose of the medication could be withheld before endoscopy with likely little harm, although this should not be considered mandatory or evidence-based. Nevertheless, it is unclear if withholding the medication for only one dose would be reliably adequate for an individual's gastric motility to return to normal. Similarly, there is insufficient evidence to suggest this practice be performed for patients taking these medications to treat diabetes, particularly because good glycemic control is important before sedation/anesthesia and endoscopy. Consequences of the ASA's preoperative suggestions are that by adding more complexity to periprocedural medication management, this may necessitate enhanced nursing resources (which

are scarce), and exacerbate barriers and care delays for patients requiring endoscopic procedures.

Generally, in patients on GLP-1 RAs who have followed standard perioperative procedures (typically an 8-hour solid-food fast and a 2-hour liquid fast) and who do not have symptoms of nausea, vomiting, dyspepsia, or abdominal distention, we advise proceeding with upper and/or lower endoscopy. In patients with symptoms suggesting possible retained gastric contents, transabdominal ultrasonography can be used to assess the stomach (if there is sufficient clinical expertise and the equipment is available) but evidence to support this modality in standard practice is lacking. In symptomatic patients for whom delaying endoscopy may have negative clinical consequences, rapid-sequence intubation is a consideration; however, this may not be possible in most ambulatory or office-based endoscopy settings. Lastly, when possible, placing patients on a liquid diet the day before sedated procedures may be a more acceptable strategy, in lieu of stopping GLP-1 RAs, and more consistent with the holistic preprocedural management of other similar conditions.

In closing, we endorse the multisociety guidance that "patient safety will always be paramount, and in the absence of actionable data, we encourage our members to exercise best practices when performing endoscopy on patients on GLP-1 RAs."[18]

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Conflicts of interest
These authors disclose the following: Christopher C. Thompson reports Consultant and Research Support from Apollo Endosurgery; Founder, Board Member, Ownership Interest with Bariendo; Founder and General Partner with BlueFlame Healthcare Venture Fund; Consultant and Research Support from Boston Scientific; Consultant with Medtronic; Founder, Board Member, Ownership Interest with ELLES; Consultant and Research Support from Endoquest Robotics; Founder, Consultant, Board Member, Ownership Interest with Enterasense Ltd; Founder, Board Member, Consultant, Ownership Interest with EnVision Endoscopy; Research Support from ERBE; Consultant, Advisory Board Member, Research Support from Fractyl; Consultant and Research Support from FujiFilm; Consultant and Research Support from GI Dynamics; Founder, Board Member, Ownership interest with GI Windows; Consultant and Research Support from Lumendi; Consultant and Research Support from Olympus/Spiration; Founder, President, Ownership Interest with Society for Metabolic and Bariatric Endoscopy; Consultant and Ownership Interest with Softac; Consultant, Advisory Board Member, Research Support from USGI Medical; and Consultant, Scientific Advisory Board, Ownership Interest with Xenter. Andrew Y. Wang declares ownership of publicly traded stock in Pfizer and GE HealthCare Technologies. The remaining author discloses no conflicts.

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