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Perioperative Fasting and Sedation in Patients Taking GLP-1 Medications: A Review of Current Research and Clinical Guidance

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Executive Summary

SedateUK has observed a high volume of inquiries regarding the use of Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RAs) in patients undergoing sedation. While GLP-1 RAs are known to delay gastric emptying, a prolonged discontinuation of several months to ensure normalized gastric emptying is generally impractical for most elective procedures.

For deep sedation and general anesthesia, the primary mitigation of aspiration risk relies on tracheal intubation with a cuffed tracheal tube, a responsibility of the anesthesiologist. For anxiolysis and moderate sedation, where airway reflexes are expected to remain intact, the aspiration risk is minimal, occurring primarily if sedation inadvertently deepens or if regurgitation is not appropriately managed. SedateUK's current recommendation, consistent with prevailing guidelines, is for patients to continue their GLP-1 RA medication and for practitioners to proceed with standard sedation protocols. Crucially, enhanced informed consent should be obtained, informing patients of the potential for increased aspiration risk and its clinical implications. To further mitigate risk, it is imperative to ensure appropriate staff training, avoid over-sedation, and maintain the ability for prompt and correct management of complications. During anxiolysis and moderate sedation, the sedation depth should not exceed moderate to preserve airway reflexes, enabling natural management of any regurgitation. This approach balances the theoretical aspiration risk with the significant disadvantages of delaying or canceling patient treatments.

Introduction

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) represent a transformative class of medications widely prescribed for the management of type 2 diabetes and obesity. A core mechanism of action for these agents is the delay of gastric emptying, which contributes significantly to their therapeutic efficacy in controlling blood glucose and promoting weight loss. However, this physiological effect introduces a critical perioperative concern: the potential for increased residual gastric contents (RGC) and, consequently, an elevated risk of pulmonary aspiration during minimal or moderate sedation, even when patients adhere to conventional fasting protocols. While aspiration is considered a rare event, its potential for severe outcomes, including significant morbidity and mortality, necessitates careful consideration in clinical practice. For deep sedation and anaesthesia, there is a potential risk of aspiration which is mitigated by intubation with a cuffed tracheal tube, so this is something now for anaesthetists to worry about for GA patients or anaesthetist delivered deep sedation. For patients who receive anxiolysis or moderate sedation (where airway reflexes remain intact), there is a small risk of aspiration, but only if the sedation turns deep inadvertently and regurgitation is not appropriately managed.

Research consistently indicates a higher prevalence of RGC in fasted patients receiving GLP-1 RAs compared to those not on these medications. Studies have reported a 30.5% to 56% higher prevalence of RGC in GLP-1 RA users despite adherence to preoperative fasting guidelines.[1] This observation, where a significant amount of gastric content remains, logically suggests an increased risk of aspiration. Yet, recent meta-analyses, while confirming the increased RGC, have not consistently demonstrated a statistically significant increase in the overall rate of pulmonary aspiration events in large cohorts.[6] This apparent discrepancy, where more gastric content is present but a higher aspiration rate is not consistently observed, implies that the clinical manifestation of delayed gastric emptying as aspiration might be mitigated by various factors. These factors could include the specific type or viscosity of the retained gastric contents (e.g., clear liquids versus solids), the effectiveness of current perioperative mitigation strategies (such as treating patients as if they have a "full stomach" with rapid sequence induction), or the inherent rarity of aspiration events, which can make detecting a statistically significant increase challenging even in large observational studies. This complex situation highlights a crucial area for further investigation: understanding the precise conditions under which increased RGC translates into actual aspiration risk and evaluating the effectiveness of current interventions in preventing these events.

Major professional societies, including the American Society of Anesthesiologists (ASA), American Gastroenterological Association (AGA), Australian and New Zealand College of Anaesthetists (ANZCA), and the Association of Anaesthetists (UK), have issued guidance on the perioperative management of GLP-1 RA patients.[2] However, a notable lack of unified

consensus persists, with recommendations for medication holding periods varying widely—from continuing the medication unchanged to suspending long-acting GLP-1 RAs for 7 to 21 days.[1] Some perspectives suggest that to truly guarantee normal gastric emptying, GLP-1 RAs would need to be stopped at least 3 months before any procedure, making pre-procedure cessation impractical unless the procedure is super-elective and the patient is willing to discontinue the medication for such an extended period. This highlights the challenge of balancing the need for an empty stomach with the long-term benefits and patient adherence to GLP-1 RA therapy, as well as the risk of cancelling or delaying treatment.[11] This divergence is not merely a disagreement but reflects the rapid clinical adoption of these drugs, the limited availability of high-quality, prospective evidence (often relying on retrospective studies, case reports, or small sample sizes), and the inherent complexity of balancing immediate perioperative aspiration risk with the long-term therapeutic benefits of continuing these medications.[1] The absence of unified, evidence-based guidance creates challenges for clinicians, potentially leading to inconsistent patient care, increased rates of elective procedure cancellations or delays, and confusion among healthcare teams. Current practices are often based on expert opinion and pragmatic consensus rather than robust clinical trial data, underscoring the urgent need for collaborative and well-designed research to provide definitive recommendations that can be widely adopted, thereby standardizing and improving patient safety. In light of these considerations, some clinicians advocate for continuing GLP-1 agonists, acknowledging that some patients may not disclose their use, and proceeding with normal sedation protocols, particularly for minimal and moderate sedation, while consenting patients for the potential aspiration risk, given its higher likelihood and severe clinical impact, including possible death.[19] This approach underscores the critical importance of appropriately trained staff who can avoid over-sedation and promptly manage complications correctly, ensuring sedation remains no deeper than moderate so that if regurgitation occurs, airway reflexes can manage the situation. This also considers the risk of cancelling patients or delaying their treatment.

In light of these complexities, patient-specific risk assessment, preoperative dietary modification (e.g., a 24-hour clear liquid diet), and the judicious use of point-of-care gastric ultrasound (POCUS) are emerging as critical strategies for individualized perioperative management. These approaches aim to minimize the risk of RGC and aspiration while striving to avoid unnecessary procedure delays or interruption of beneficial long-term therapy.

GLP-1 Receptor Agonists and Perioperative Safety

Overview of GLP-1 RAs: Mechanism of Action, Indications, and Common Medications

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), also known as incretin mimetics, constitute a class of medications that emulate the action of the natural incretin hormone, GLP-1. This hormone is physiologically secreted by intestinal L cells following food intake.[1] The primary mechanism by which these agents operate involves enhancing glucose-dependent insulin secretion from pancreatic beta cells and simultaneously inhibiting glucagon release from alpha cells, leading to a reduction in blood glucose levels.[1] A particularly significant aspect for perioperative care is that GLP-1 RAs also substantially delay gastric emptying, diminish food intake, and suppress appetite through their effects on the hypothalamus and via vagal afferents.[1] This multifaceted action contributes to both improved glycemic control and notable weight reduction.[1]

Initially approved for the treatment of type 2 diabetes mellitus (T2DM), the therapeutic scope of GLP-1 RAs has broadened to encompass weight management in individuals who are obese or overweight. Furthermore, some of these medications have demonstrated significant cardiovascular benefits.[1] Commonly prescribed GLP-1 RAs include Exenatide (Byetta, Bydureon), Liraglutide (Victoza, Saxenda), Dulaglutide (Trulicity), Semaglutide (Ozempic, Wegovy, Rybelsus), and Tirzepatide (Mounjaro), the latter being a dual GIP/GLP-1 receptor agonist.[18] The frequency of administration varies across these agents, with Liraglutide typically given daily, while Dulaglutide, subcutaneous Semaglutide, and Tirzepatide are administered weekly. An oral formulation of Semaglutide is also available for daily use.[21]

The Physiological Effect of GLP-1 RAs on Gastric Emptying and its Implications for Sedation

The delay in gastric emptying is a well-recognized and intentional pharmacological effect of GLP-1 RAs, integral to their effectiveness in glycemic control and weight loss.[1] This delay can be clinically significant; for instance, a meta-analysis indicated a 36-minute delay in gastric emptying for solids.[7] Under normal physiological conditions, gastric emptying of clear liquids is relatively rapid, with 500 mL of water emptying in approximately 20 minutes. However, this process is considerably slowed by higher caloric intake, proteins, and especially lipids.[1] GLP-1 RAs intensify this slowing effect by inhibiting gastrointestinal motor function through both central and vagal pathways.[3]

The core mechanism of GLP-1 RAs—delaying gastric emptying—is a designed therapeutic effect that contributes to their efficacy in managing diabetes and promoting weight loss.[1] However, in the perioperative context, this very same mechanism transforms into a significant unintended safety risk. An empty stomach is paramount for safe sedation, particularly to minimize the risk of aspiration.[2] This inherent conflict highlights a fundamental challenge in modern medicine, where a drug's beneficial action in one physiological context becomes a liability in another. It underscores the necessity for clinicians to conduct a meticulous risk-benefit analysis for each patient, moving beyond a simplistic "stop or continue" decision. The goal is to devise strategies that maintain the long-term health benefits of GLP-1 RA therapy while effectively mitigating the acute, procedure-related aspiration risk, especially for procedures involving minimal or moderate sedation.

The Concern of Pulmonary Aspiration During Minimal or Moderate Sedation in GLP-1 RA Users

The primary perioperative concern arising from delayed gastric emptying is the increased risk of residual gastric contents (RGC) despite adherence to standard preoperative fasting protocols.[3] The presence of RGC substantially elevates the risk for regurgitation of stomach contents and subsequent aspiration into the airways and lungs during sedation. While airway reflexes are generally maintained during minimal and moderate sedation, there is a small but critical risk of aspiration if the sedation inadvertently deepens and regurgitation is not appropriately managed.[19] Pulmonary aspiration is a serious and potentially life-threatening complication, capable of leading to severe pneumonitis, aspiration pneumonia, acute respiratory distress syndrome, prolonged hospitalization, long-term morbidity, and even death.[20]

The extended half-lives of certain GLP-1 RAs, particularly semaglutide (which can be up to 7 days, requiring approximately 21 days for clearance based on three half-lives), mean that the drug's effect on gastric emptying can persist for a considerable duration even after the last dose has been administered.[3] This prolonged pharmacological effect significantly complicates traditional short preoperative fasting protocols (e.g., 6-8 hours for solids, 2 hours for clear liquids). Simply adhering to standard fasting times is likely insufficient to normalize gastric emptying, which is consistent with the observed high rates of residual gastric contents in fasted GLP-1 RA users.[1] This necessitates either significantly longer holding periods for the medication, which can introduce other risks like hyperglycemia or rebound weight gain, or the implementation of more dynamic and individualized mitigation strategies, such as dietary modifications and objective gastric content assessment, especially when aiming to keep sedation at minimal or moderate levels.

Current Preoperative Fasting Guidelines and Recommendations

Standard Fasting Guidelines (American Society of Anesthesiologists - ASA)

For healthy patients undergoing elective procedures, the American Society of Anesthesiologists (ASA) generally recommends specific minimum fasting periods. These include 2 hours for clear liquids, 4 hours for human breast milk, 6 hours for non-human milk, formula milk, and light meals, and 8 hours for fried or fatty solids or meat.[1] It is widely acknowledged that actual fasting times frequently exceed these minimums due to various logistical considerations and cultural influences.[1]

Guidelines for GLP-1 RA Patients from Major Professional Societies

The emergence of GLP-1 RAs has prompted several professional societies to issue guidance on their perioperative management, reflecting a growing awareness of the unique challenges these medications pose. While much of the guidance specifically addresses general anesthesia and deep sedation, the principles of managing gastric emptying risk are also highly relevant for procedures involving minimal or moderate sedation, where inadvertent deepening of sedation could compromise airway reflexes.

- ### American Society of Anesthesiologists (ASA)

The initial consensus guidance released by the ASA in 2023 recommended discontinuing daily GLP-1 RAs on the day of the procedure and weekly GLP-1 RAs one week prior to surgery.[1] If patients presented with gastrointestinal (GI) symptoms such as nausea, vomiting, abdominal pain, shortness of breath, or constipation, or if the medication was not held as advised, the guidance suggested postponing surgery and discussing the associated risks with the patient.[1] For asymptomatic patients who had not held their medication, the decision to proceed could be guided by a point-of-care gastric ultrasound assessment.[1]

More recent multi-society guidance, involving the ASA, American Gastroenterological Association, and American Society for Metabolic and Bariatric Surgery, suggests a more nuanced approach: most patients should continue their GLP-1 RAs before elective surgery.[11] For patients identified as being at highest risk—such as those in the dose escalation phase, experiencing significant GI symptoms, on higher doses, or with other conditions like Parkinson's disease—a liquid diet for 24 hours before the procedure or other tailored measures are recommended.[11] The ASA guidance explicitly notes a lack of definitive evidence to suggest optimal fasting durations specifically for GLP-1 RA patients.[2]

- American Gastroenterological Association (AGA)

The AGA Institute's Rapid Clinical Practice Update indicates that endoscopic procedures generally do not need to be postponed for patients without GI symptoms.[13] They advise proceeding with upper and/or lower endoscopy for patients on GLP-1 RAs who have followed standard perioperative fasting guidelines (typically an 8-hour solid-food fast and a 2-hour liquid fast) and who do not exhibit symptoms of nausea, vomiting, dyspepsia, or abdominal distention.[12] The AGA considers placing patients on a liquid-only diet for 24 hours before the procedure as a more acceptable strategy than discontinuing GLP-1 RAs.[12] Furthermore, the AGA notes that while withholding GLP-1 RAs solely for weight loss may be safe and reasonable, it should not be considered mandatory or evidence-based. For diabetic patients, withholding these medications might pose more risk than benefit.[11] This guidance is particularly relevant for procedures performed under minimal or moderate sedation, where maintaining patient comfort while minimizing aspiration risk is key.

- Australian and New Zealand College of Anaesthetists (ANZCA)

The ANZCA's recommendations state that elective preprocedural cessation of GLP-1 RAs is not recommended, citing risks of hyperglycemia in diabetic patients and potential compromise of weight control.[17] They recommend preprocedural diet modification, specifically a 24-hour clear fluid diet, followed by standard 6-hour fasting.[17] The guidance also suggests that omission of longer-acting GLP-1 RAs for 1-2 weeks is unlikely to significantly alter gastric emptying.[17] For shorter-acting GLP-1 RAs, such as liraglutide, continuation is recommended, though withholding for 3-4 days may be considered in individual circumstances, acknowledging potential implications for glycemic control and weight management.[17] These recommendations apply to sedation for endoscopic procedures as well as general anesthesia.[17]

- Association of Anaesthetists (UK)

For diabetic patients, the Association of Anaesthetists (UK) suggests considering continuation of GLP-1 RA treatment to avoid glycemic exacerbation.[30] For non-diabetic patients, a cessation period appropriate to the half-life of the agent (e.g., at least three half-lives) may be considered.[19] In cases of significant gastrointestinal symptoms, delaying elective surgery is advised; otherwise, patients should be managed as if they have an unfasted or "full stomach".[30] They also propose considering an extended fasting period (e.g., 24 hours), a clear fluid regimen, or a residue-free diet before surgery, particularly for patients unable to cease GLP-1 RA treatment in a timely manner.[30] A multidisciplinary consensus statement from several UK bodies, including the Association of Anaesthetists, recommends continuing GLP-1 RAs before surgery, coupled with full risk assessment and stratification, and the application of

perioperative techniques to mitigate aspiration risk.[16]

- Society for Perioperative Assessment and Quality Improvement (SPAQI)

The Society for Perioperative Assessment and Quality Improvement (SPAQI) has published a multidisciplinary consensus statement, developed through a modified Delphi process and supported by a systematic review. This statement provides updated recommendations for perioperative GLP-1 RA management and preoperative fasting times for both solids and liquids.[6]

Analysis of Variations and Points of Consensus/Divergence

The guidelines from various professional societies reveal both significant divergences and emerging areas of consensus regarding the perioperative management of patients on GLP-1 RAs. The most notable variation lies in the recommended medication holding periods, which range from continuing the medication unchanged (as suggested by ANZCA, AGA, and some multi-society guidance) to specific daily/weekly holding periods (from initial ASA guidance) and even extended periods of 3 weeks for semaglutide (based on its half-life).[1]

This evolving guidance reflects a maturing understanding of the complex risk-benefit profile of GLP-1 RAs in the perioperative setting. It signifies a move beyond a singular focus on aspiration risk to a more holistic consideration of the patient's overall health and the importance of maintaining chronic disease management. Initial ASA guidance leaned towards withholding GLP-1 RAs.[1] However, subsequent multi-society guidance, including the ASA, shifted to recommend that most patients should continue their GLP-1 RAs.[11] The explicit rationale for this shift includes avoiding the risks of hyperglycemia in diabetic patients and preventing the reversal of weight loss benefits in others.[11] This indicates a growing trend towards nuanced, individualized decision-making where long-term therapeutic goals are carefully balanced against acute procedural risks, moving away from blanket "stop-all" approaches.

Despite the divergences, several common themes and emerging points of consensus are evident:

- Universal Acknowledgment: There is universal acknowledgment of the delayed gastric emptying effect of GLP-1 RAs and the associated aspiration risk, relevant across all levels of sedation.[1]
- Individualized Risk Assessment: Strong emphasis is placed on individualized risk assessment, particularly for patients exhibiting GI symptoms, those in the dose escalation phase, on higher doses, or with pre-existing comorbidities that affect gastric emptying.[11]
- Role of Point-of-Care Gastric Ultrasound (POCUS): The increasing and critical role of point-of-care gastric ultrasound in assessing stomach contents and guiding clinical

decisions is consistently highlighted, offering a real-time assessment that is valuable for all sedation levels.[1]

- 24-hour Clear Liquid Diet: A frequent recommendation is a 24-hour clear liquid diet prior to surgery as a mitigation strategy, applicable to procedures under minimal or moderate sedation.[11]
- "Full Stomach" Precautions: A consistent recommendation is to treat patients as having a "full stomach" and manage accordingly if GLP-1 RAs were not held as advised, or if RGC is suspected or confirmed.[12] For minimal and moderate sedation, this translates to heightened vigilance, careful titration of sedatives to maintain airway reflexes, and readiness to manage regurgitation or deepening of sedation.

While some guidelines suggest prolonged holding periods for weekly GLP-1 RAs (e.g., 7 days or even 21 days for semaglutide based on half-life), other societies and more recent guidance emphasize practical alternatives like a 24-hour liquid diet.[1] This shift may be driven by the recognition of the logistical challenges and potential for patient non-compliance with very long holding periods, as well as the adverse effects of stopping the medication.[11] This suggests that clinical practice is moving towards pragmatic solutions that prioritize patient safety while acknowledging the realities of patient adherence and the benefits of ongoing therapy. The increasing emphasis on preoperative liquid diets and POCUS indicates a transition from rigid, time-based fasting rules to a more dynamic, real-time assessment and management strategy. This approach recognizes that simply extending fasting duration may not be the most effective or patient-centric solution for managing the unique gastric emptying delays caused by GLP-1 RAs, particularly for procedures where deep sedation or general anesthesia may not be the primary goal.

Consideration of Hospital-Specific Protocols

Despite the issuance of national and international guidelines, the extent to which individual hospitals and health systems, such as those within the U.S. Military Health System, have implemented consistent policies remains unclear.[2] Barriers to system-wide policy implementation include a lack of gastric ultrasound practice and comfort among clinicians, reported skill and knowledge gaps, pressure not to cancel cases, and scheduling challenges.[2] Consequently, some hospitals have developed specific patient guides with strict fasting instructions, often emphasizing clear liquids and explicitly warning of procedure delays or cancellations if instructions are not followed.[31]

Table 1: Comparative Summary of Major Professional Society Guidelines for Perioperative GLP-1 RA Management

Society/Organization	Recommendation on Medication Holding	Recommendation on Preoperative Diet Modification	Role of Gastric Ultrasound (POCUS)	Guidance for Symptomatic Patients	Rationale/Key Considerations
ASA (Initial 2023)	Daily: Hold day of surgery. Weekly: Hold 1 week prior.	Standard fasting guidelines.	Recommended for decision-making if medication not held or GI symptoms present.	Delay surgery; discuss risks. Treat as "full stomach".	Lack of evidence for optimal fasting duration.
ASA (Multi-Society Guidance)	Most patients: Continue. High risk: Defer elective surgery until escalation phase passes/GI symptoms dissipate.	High risk: Liquid-only diet for 24 hours.	Recommended for assessing stomach contents in high-risk patients.	Wait until symptoms dissipate; defer surgery.	Balance benefit of continuing drug with aspiration risk; avoid hyperglycemia/weight rebound. Avoid bias.
AGA	Generally: Do not postpone for asymptomatic patients. Withholding for weight loss: Safe/reasonable but not mandatory. For diabetes: Withholding may pose more risk than benefit.	Standard fasting; consider 24-hour liquid diet.	Not explicitly mentioned in available snippets, but implied by multi-society guidance.	Proceed with caution, consider rapid-sequence intubation if delay harms.	Avoid unnecessary delays; balance risks/benefits.
ANZCA	Elective cessation: Not recommended. Long-acting: Omission for 1-2 weeks unlikely to alter gastric emptying. Short-acting (e.g., liraglutide): Continue; 3-4 day hold may be considered.	24-hour clear fluid diet, followed by standard 6-hour fasting.	Recommended for determining gastric contents.	Manage as unfasted; risk mitigation strategies necessary.	Risks of hyperglycemia/compromised weight control. Insufficient data to support cessation.
Association of Anaesthetists (UK)	Diabetic: Consider continuing. Non-diabetic: Consider cessation for ≥3 half-lives.	Extended fasting (e.g., 24 hours), clear fluid regimen, or residue-free diet.	Consider for risk stratification.	Delay elective surgery; otherwise, manage as unfasted ("full stomach").	Avoid glycemic exacerbation.
SPAQI	Provides updated recommendations for medication management (details not in snippets).	Provides updated recommendations for fasting times (details not in snippets).	Not explicitly mentioned in available snippets, but scope includes perioperative management.	Not explicitly mentioned in available snippets, but scope includes perioperative management.	Multidisciplinary consensus based on systematic review.

Note: This table summarizes information from the provided research snippets. For complete and most up-to-date guidelines, refer to the full publications from each respective society.

Evidence Base: Residual Gastric Contents and Aspiration Risk in GLP-1 RA Users

Studies on the Prevalence of Increased Residual Gastric Contents (RGC)

Multiple observational studies consistently report an increased prevalence of residual gastric contents (RGC), typically defined as solids, thick liquids, or clear liquids greater than 1.5 mL/kg, in patients taking GLP-1 RAs. This phenomenon occurs even after these patients adhere to standard preoperative fasting guidelines, when compared to control groups not on these medications.[2] A significant cross-sectional study from UTHealth Houston revealed that 56% of patients on GLP-1 RAs exhibited substantial gastric contents on gastric ultrasound prior to an elective procedure, despite diligently following recommended fasting protocols. This incidence was considerably higher than the 19% observed in non-users, representing an adjusted prevalence ratio of 2.48, or a 30.5% higher prevalence in the GLP-1 RA group.[1] Another study focusing on esophagogastroduodenoscopies (EGDS) performed under general anesthesia reported an increase in residual gastric content in 6.7% of GLP-1 RA patients, with a notably higher proportion (24.2%) specifically observed in the semaglutide group.[3]

The risk of impaired gastric emptying (IGE) appears to be highest early in therapy, with a median onset for semaglutide reported at 40.5 days. This "early failure" pattern might be consistent with tachyphylaxis, suggesting a reduced drug response on gastric emptying after prolonged exposure.[20] However, it is crucial to note that the assumption of tachyphylaxis leading to normal gastric emptying with sustained administration of longer-acting GLP-1 RAs is not supported by existing evidence.[17] While some studies suggest that withholding GLP-1 RAs for less than 2 weeks or the presence of presurgical digestive symptoms increases the probability of RGC [2], other smaller studies have found no significant variation in RGC based on the duration of medication holding.[2] One retrospective study indicated that gastrointestinal symptoms such as nausea, vomiting, dyspepsia, and bloating might only resolve after a time interval of 14 days or more, without a clear association with RGC reduction.[3]

Review of Reported Aspiration Events and Case Series

Although the overall risk of aspiration during any level of sedation is considered low, its precise understanding in the context of GLP-1 RA use remains incomplete.[1] Several anecdotal reports and case series have documented pulmonary aspiration events in patients taking GLP-1 RAs, some of whom reportedly adhered to appropriate fasting protocols.[10] These reports serve as critical safety signals, highlighting the potential for adverse outcomes. The severity of these reported events can be significant, including instances of reported death, hospitalizations, and life-threatening conditions.[20] Specific examples include a 42-year-old patient on semaglutide

who was found to have gastric content during endoscopy despite an 18-hour fast [18], and another patient who regurgitated a large volume of clear gastric contents upon induction of anesthesia despite stopping semaglutide 2 days prior.[19] Another documented case involved the presence of food from 2-3 days prior being found in the stomach.[23] While many reported cases involve general anesthesia or deep sedation, the underlying risk of RGC means that even in minimal or moderate sedation, vigilance is required to prevent inadvertent deepening of sedation that could compromise airway reflexes and lead to aspiration.

Analysis of Systematic Reviews and Meta-analyses on the Association between GLP-1 RA Use and Pulmonary Aspiration

Recent systematic reviews and meta-analyses have attempted to synthesize the available evidence on the association between GLP-1 RA use and perioperative aspiration. A systematic review and meta-analysis by Elkin et al., which pooled data from 9 observational studies involving 304,060 individuals with 481 aspiration cases, found that GLP-1 RA exposure was not statistically associated with pulmonary aspiration (Odds Ratio, 1.04; 95% Confidence Interval [CI], 0.87-1.25). However, the certainty of this evidence was rated as low.[8] The same meta-analysis, consistent with other studies, confirmed a positive association between GLP-1 RA exposure and increased RGC despite appropriate fasting (OR, 5.96; 95% CI, 3.96-8.98), also with low certainty evidence.[8]

Another comparative cohort study found no increased risk of pulmonary aspiration during upper gastrointestinal endoscopy among adults with type 2 diabetes using GLP-1 RAs when compared with SGLT-2 inhibitors (pooled risk ratio 0.98, 95% CI 0.73 to 1.31).[6] SGLT-2 inhibitors were chosen as a comparator because they are used for similar indications but are not known to affect gastric emptying, making them an appropriate reference group.[10] It is important to note that many of these studies and meta-analyses include procedures performed under general anesthesia or deep sedation, where the risk of aspiration is inherently higher due to compromised airway reflexes. The findings, however, still underscore the presence of RGC, which is a foundational risk factor regardless of the depth of sedation.

Discussion of the Discrepancy between Increased RGC and the Observed Aspiration Rate

The consistent finding of increased RGC in GLP-1 RA users [1] stands in apparent contrast to the meta-analysis findings of no statistically significant increase in the overall rate of aspiration events.[6] This discrepancy suggests several possibilities. While the physiological potential for aspiration is higher due to the presence of RGC, actual aspiration events might remain rare due to effective perioperative management strategies. Clinicians may be proactively treating these patients as if they have a "full stomach," employing rapid sequence induction (for deeper sedation/GA), or carefully selecting patients for procedures based on risk assessment.[20] For

minimal and moderate sedation, this means meticulous titration of sedatives to ensure airway reflexes remain intact and prompt intervention if sedation deepens inadvertently. Additionally, the inherent rarity of aspiration events makes it challenging to detect a statistically significant increase, even in large observational studies. Furthermore, the nature of the retained contents (e.g., primarily clear liquids versus solids) might influence the clinical impact of aspiration. This complex situation highlights a critical knowledge gap: understanding the precise conditions under which increased RGC translates into actual aspiration risk, and the effectiveness of current interventions in preventing these events, particularly in the context of minimal and moderate sedation where maintaining patient safety relies heavily on preserved airway reflexes.

Conclusion

The research on fasting times for minimal and moderate sedation in patients taking GLP-1 medications reveals a complex and evolving landscape. There is unequivocal evidence that GLP-1 receptor agonists significantly delay gastric emptying, leading to a higher prevalence of residual gastric contents even after standard preoperative fasting. This physiological effect inherently raises concerns about pulmonary aspiration during sedation, particularly if minimal or moderate sedation inadvertently deepens and protective airway reflexes are compromised. Despite the consistent finding of increased residual gastric contents, large-scale meta-analyses have not yet demonstrated a statistically significant increase in the overall rate of aspiration events in GLP-1 RA users compared to control groups. This apparent paradox suggests that while the risk potential is elevated, current perioperative management strategies, such as careful patient selection, meticulous titration of sedatives, and readiness to manage a "full stomach" scenario, may be effectively mitigating actual aspiration events. The lack of a unified consensus across major professional societies regarding specific medication holding periods underscores the challenges posed by the rapid adoption of these drugs and the limited availability of high-quality, prospective clinical trial data. While some guidelines initially favored specific holding periods, a shift towards continuing GLP-1 RAs for most patients reflects a growing understanding of the importance of balancing acute perioperative risks with the long-term therapeutic benefits of these medications, such as glycemic control and weight management. For minimal and moderate sedation, this often means continuing the medication while implementing other risk mitigation strategies.

Moving forward, individualised patient assessment is paramount. This includes a thorough evaluation of gastrointestinal symptoms, the patient's phase of GLP-1 RA therapy (e.g., dose escalation), and the presence of other comorbidities affecting gastric emptying. The increasing reliance on point-of-care gastric ultrasound to objectively assess stomach contents prior to procedures is a critical advancement, enabling real-time, dynamic decision-making. Furthermore, the recommendation for a 24-hour clear liquid diet before surgery is a practical and increasingly adopted mitigation strategy. For minimal and moderate sedation, it is crucial that staff are appropriately trained to avoid over-sedation and can promptly manage complications correctly, ensuring that sedation remains no deeper than moderate so that if regurgitation occurs, the patient's airway reflexes can manage the situation. Patients should be warned and consented for the potential aspiration risk, given the higher likelihood of RGC and the potential clinical impact, including possible death. To bridge the existing knowledge gaps and establish definitive, evidence-based guidelines, high-quality prospective studies and randomised controlled trials are urgently needed. Such research will provide a clearer understanding of the optimal fasting durations, the true incidence of aspiration, and the most effective perioperative management strategies for patients on GLP-1 RAs undergoing minimal and moderate sedation, ultimately leading to standardized, safer patient care.

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