Perioperative Anesthetic Implications of Tirzepatide (Mounjaro) in Saudi Arabia

ABSTRACT

Tirzepatide, a dual GIP and GLP-1 receptor agonist, is now a leading therapeutic choice for type 2 diabetes mellitus and obesity because it reduces glycated hemoglobin (HbA1c) and body weight more effectively than previous GLP-1 receptor agonists. Its general adoption, Saudi Arabia included, demonstrates its strengths in glycemic control and weight loss. The relationship between GLP-1 receptor agonists and retained gastric content, regurgitation, and bronchoaspiration, despite standard fasting, was evaluated using randomized trials, meta-analyses, and clinical guidelines. Vagally mediated reductions in gastric motility are discussed as a mechanistic pathway along with the additive effects of sedatives and opioids. Clinical data and surgical audits reveal unforeseen airway problems, which sometimes call for adjusted anesthesia starts, quick sequence procedures, and on occasion, delayed surgeries. The guidelines currently in place both internationally and regionally offer various approaches to stopping medication before elective surgery, from all patients stopping to individual assessments informed by point-of-care gastric ultrasound. As utilization expands quickly in Saudi Arabia, balancing less aspiration risk and prevented metabolic instability is particularly key. This review emphasizes the demand for greater perioperative alertness, collaborative multidisciplinary efforts, and customized local procedures to maximize patient safety in this developing treatment space.

Keywords: Tirzepatide, GLP-1 agonists, anesthesia, delayed stomach emptying, aspiration risk, Saudi Arabia

INTRODUCTION

Tirzepatide, acting on both GIP and GLP-1 receptors, lowered HbA1c and body weight more than semaglutide and dulaglutide. While tirzepatide binds the GIP receptor, its GLP-1 receptor affinity is roughly five times weaker compared to endogenous GLP-1. Medicines called glucagon-like peptide-1 receptor agonists are for patients affected by type 2 diabetes mellitus and obesity. The drugs are indicated for initial type 2 diabetes mellitus treatment, particularly for individuals who are obese, and/or at high risk for atherosclerotic cardiovascular disease, heart failure or chronic kidney disease. These treatments are effective for reducing fasting plasma glucose and glycated haemoglobin in individuals with type 2 diabetes. These drugs pose a low hypoglycaemia risk and have no clinically meaningful difference in hypoglycaemic events among drugs in their class. Trials suggest these are effective at encouraging weight loss by prolonging stomach processing and boosting satiety, both for patients with and without diabetes [1]. Clinical use of GLP-1

receptor agonists began in the mid-2000s. These consist of exenatide, lixisenatide, liraglutide, dulaglutide, and semaglutide. The frequency is twice daily (standard-release exenatide), daily (liraglutide, lixisenatide, or oral semaglutide), or weekly (extended-release exenatide, dulaglutide, or s.c. semaglutide). They must be given s.c. because they are polypeptides, with the exception of oral semaglutide. They imitate what the body's GLP-1 does [2]. Globally, GLP-1RAs, drugs for blood sugar and weight loss, are becoming more common [3]. Nationwide, anaesthesiologists are primarily concerned about aspiration risk during general anesthesia in patients on glucagon-like peptide-1 agonists, due to delayed gastric emptying. New clinical guidance from the American Society of Anesthesiologists recommends that most patients continue their glucagon-like peptide-1 (GLP-1) receptor agonists before elective surgery [4]. The USA approved Tirzepatide in May 2022, which was its first approval, to help adults with type 2 diabetes mellitus manage their blood sugar levels. Tirzepatide was given the green light by the FDA in November 2023 for managing weight over the long term in adults dealing with obesity [5].

The use of GLP-1RAs, medications for blood sugar and weight loss, is growing globally [3]. The last 20 years have seen a major increase in the use of glucagon-like peptide-1 receptor agonists, especially in the Gulf. Saudi Arabia has seen a big increase in prescriptions for

diabetes and weight loss [6].

Percent of time patients are evaluated at a preoperative anaesthesia clinic	**n**	**% of total**
<25% of the time	332	18.85%
25-50% of the time	265	15.05%
50-75% of the time	355	20.16%
75-100% of the time	454	25.78%
Never	355	20.16%
Supervision of midlevel providers (residents, nurse anaesthetists, anaesthesia assistants)	**n**	**% of total**
No	383	21.75%
Yes	1378	78.25%
Average BMI in practice region	**n**	**% of total**
<25	21	1.20%
>40	29	1.66%
25-30	219	12.53%
30-35	1021	58.41%
35-40	458	26.20%
BMI cut-off for elective surgical procedures	**n**	**% of total**
No BMI cut-off	1360	77.36%
Yes, <30	3	0.17%
Yes, <35	8	0.46%
Yes, <40	56	3.19%
Yes, <45	102	5.80%
Yes, <50	229	13.03%
Familiarity with a class of drugs called GLP-1 agonists (i.e., Ozempic, Wegovy, Mounjaro)	**n**	**% of total**

Most common indication for which patients have been prescribed a GLP-1 agonist	n	% of total
Cosmetic weight loss	128	8.36%
Primary diabetes management	903	58.94%
Primary obesity management	350	22.85%
Unknown	151	9.86%
BMI, body mass index; GLP-1, glucose-dependent insulinotropic peptide.		

Table 1. Patient Population/Practice Information [6].

Medical trend analysis shows growing use due to provider/patient awareness of benefits for blood sugar and weight. Patient behavior in the region shows that many start therapy on a specialist's advice, but some are swayed by social media and health drives [6].

Delayed gastric emptying is a known effect of GLP-1-RAs. Consequently, recent case reports and studies, though not definitive, indicate perioperative GLP-1-RAs might elevate bronchoaspiration risk, despite fasting guidelines being met or surpassed [7]. National anaesthesiologists identified their primary concern for patients on glucagon-like peptide-1 agonists as a heightened risk of aspiration during general anaesthesia, due to delayed gastric emptying [6]. Several Anesthesiology Societies have published guidelines and safety bulletins, which is a result [7]. New clinical guidance from the American Society of Anesthesiologists suggests that most patients should continue using GLP-1 receptor agonists before elective surgery [4]. The use of GLP-1-RAs during the preoperative period also appears to increase the risk of bronchial aspiration and delayed gastric emptying[7].

Pharmacological Profile

Tirzepatide (Mounjaro®), a novel dual incretin agonist targeting GIP and GLP-1 receptors, is approved alongside diet and exercise to improve blood sugar control in adults with T2DM, offered in prefilled single-dose pens and vials. Adults with poorly managed type 2 diabetes (T2DM) saw better blood sugar control and weight loss with once-weekly subcutaneous tirzepatide, alone or with other diabetes medications, compared to GLP-1 receptor agonists (Dulaglutide 0.75 mg and Semaglutide 1 mg), with basal and placebo insulin, according to the Phase 3 SURPASS trial. Tirzepatide was typically tolerated well, showing a safety profile similar to GLP-1 receptor agonists. The risk of severe hypoglycemia was low with tirzepatide, and there was no increased risk of major cardiovascular problems. Effects ranged in intensity from minor to average, the most frequent being gastrointestinal, like nausea, diarrhea, anorexia, and vomiting [8].

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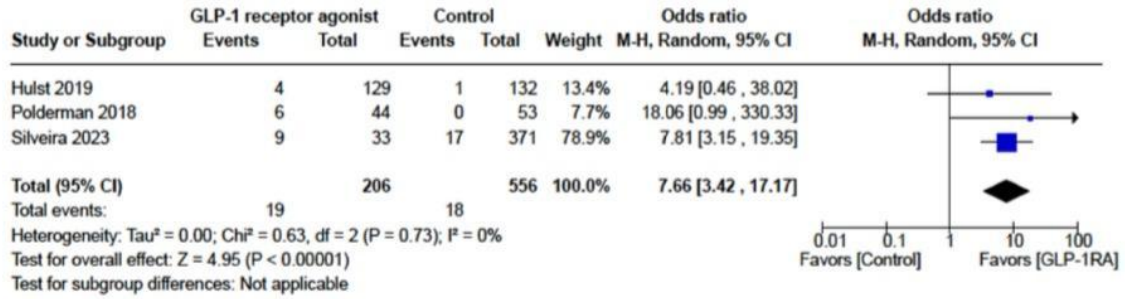
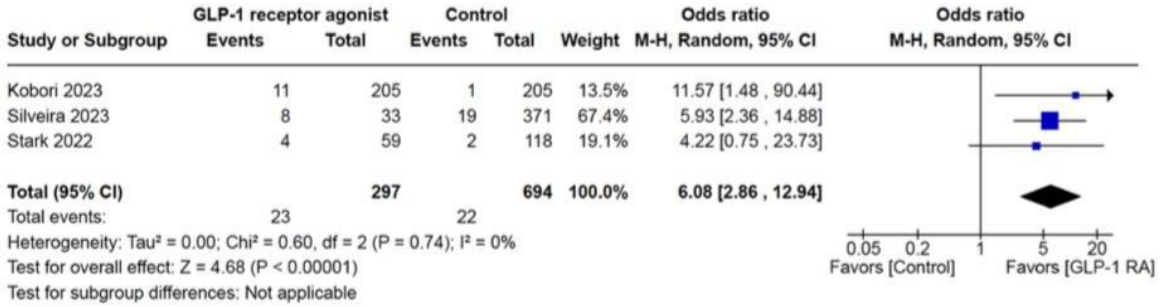
89 **Delayed Gastric Emptying & Retained Gastric Content in GLP-1RA Users**

90 The findings of a recent systematic review and meta-analysis of 14 studies (2143 patients)
91 indicate that gastrointestinal symptoms and retained gastric content are common in GLP-
92 1RA users who adhere to standard preoperative fasting guidelines [3].

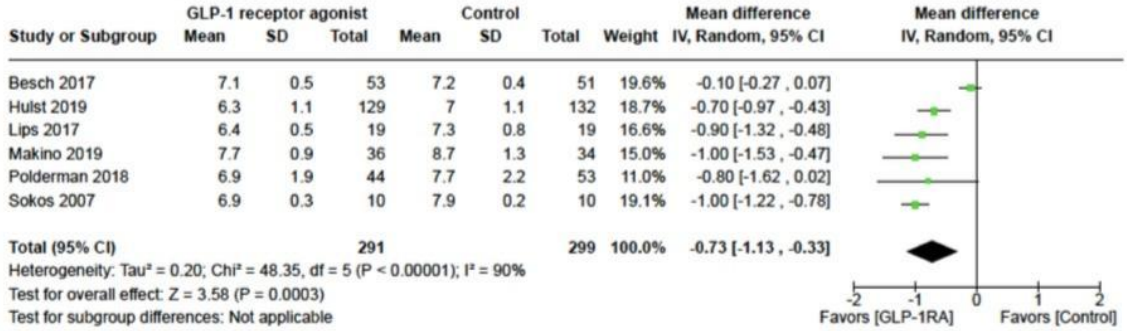
GLP-1RAs were associated with an increased rate of pre-procedural GI symptoms



GLP-1RAs resulted in an expressive increase in RGC compared to the control



GLP-1RAs improved glycemic control



Subgroup with 100% diabetics. GLP-1RAs improved glycemic control with zero heterogeneity

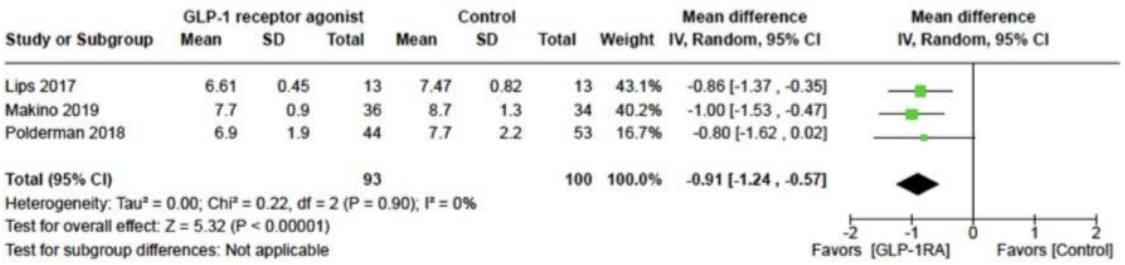


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Fig.1 Study outcomes: GLP-1RAs were associated with an increased rate of pre-procedural GI symptoms, GLP-1 RAs resulted in an expressive increase in RGC compared to the control, GLP-1RAs improved glycemic control, and subgroup with 100% diabetics and GLP-1RAs improved glycemic control with zero heterogeneity [3].

Compared to non-users, this study found that GLP-1RAs were linked to more delayed gastric emptying and residual volume, and issues like nausea [3]. Surgical observations confirmed these results; extended fasting did not remove stomach contents in these patients [7]. Retrospective analyses showed a link between this and increased regurgitation and aspiration risk during anesthesia induction [4]. Case reports back up the clinical concern; patients on GLP-1RAs had considerable stomach contents during procedures, questioning fasting guidelines [6]. Some centers use point-of-care gastric ultrasound to assess patients before surgery, showing a substantial group with a "full stomach" despite adequate fasting [9]. Targeted assessment before surgery and possibly adjusted fasting for patients taking GLP-1RAs are crucial, as shown by these findings [10].

Reference	Age (y)	Male %	Race/Ethnicity %	BMI (kg/m^2)	DM %	GLP-1 RA Dose	GLP-1 RA Route	Findings
[25]	50.8	51.5	-	26.2	9.4	-	Subcutaneous	RGCs in the GLP-1 RA vs. control group (24.2% vs. 5.1%, $p < 0.001$), only 1 aspiration event in the GLP-1 RA group
[28]	65	88.5	-	33	97.5	-	Subcutaneous	RGCs in the GLP-1 RA vs. control group (6.8% vs. 1.7%, $p = 0.08$)
[29]	60.9	35.8	-	35.2	76.7	-	Subcutaneous or oral	RGCs (9.4%), aspiration (0.1%)
[30]	-	-	-	-	-	-	-	4.8 aspiration cases per 10,000 endoscopies
[31]	44	10.5	-	40.1	35.1	Semaglutide 0.25–2.4 mg/week Liraglutide 0.6–3 mg/day Dulaglutide 0.75–4.5 mg/week Tirzepatide 2.5–15 mg/week	Subcutaneous	No cases of RGCs or pulmonary aspiration
[32]	54	41	White 91 Hispanic 5 Black 2	30.7	18	-	-	RGCs in the GLP-1 RA vs. control group (13.6% vs. 2.3%, $p < 0.0001$), only 1 aspiration event in the control group
[33]	53.94	29.8	White 60.1 Black 39.9	35.96	85.7	-	-	RGCs in the GLP-1 RA vs. control group (13.1% vs. 4.8%, $p = 0.025$)
[34]	56	45	-	-	100	-	-	Aspiration in the GLP-1 RA, dipeptidyl peptidase 4 inhibitor, and chronic opioid users (0.05% vs. 0.07% vs. 0.11%)
[35]	60.7	42.3	Caucasian 53.9 African American 19.6 Hispanic 17.5 Asian 3.1	-	82.5	-	Subcutaneous or oral	RGCs (8.6%)
[36]	61.5	50.5	-	32.45	88	-	Subcutaneous or oral	RGCs in the GLP-1 RA vs. control group (14% vs. 4%, $p < 0.01$), no aspiration events
[37]	61.3	42.5	-	34	47	-	-	RGCs in the GLP-1 RA vs. control group (18.7% vs. 4.9%, $p = 0.004$), 1 aspiration event in the GLP-1 RA group vs. 0 in the control group
[38]	60	63.1	-	-	85.6	-	-	RGCs in the regular diet vs. clear liquid/low-residue diet groups (10% vs. 1.5%, $p = 0.03$), no aspiration events

BMI—body mass index, y—years, kg/m^2—kilograms divided by height in meters squared, DM—diabetes mellitus, RGCs—retained gastric contents.

Table 2. Major clinical studies evaluating GLP-1 RA effects on upper endoscopy [10].

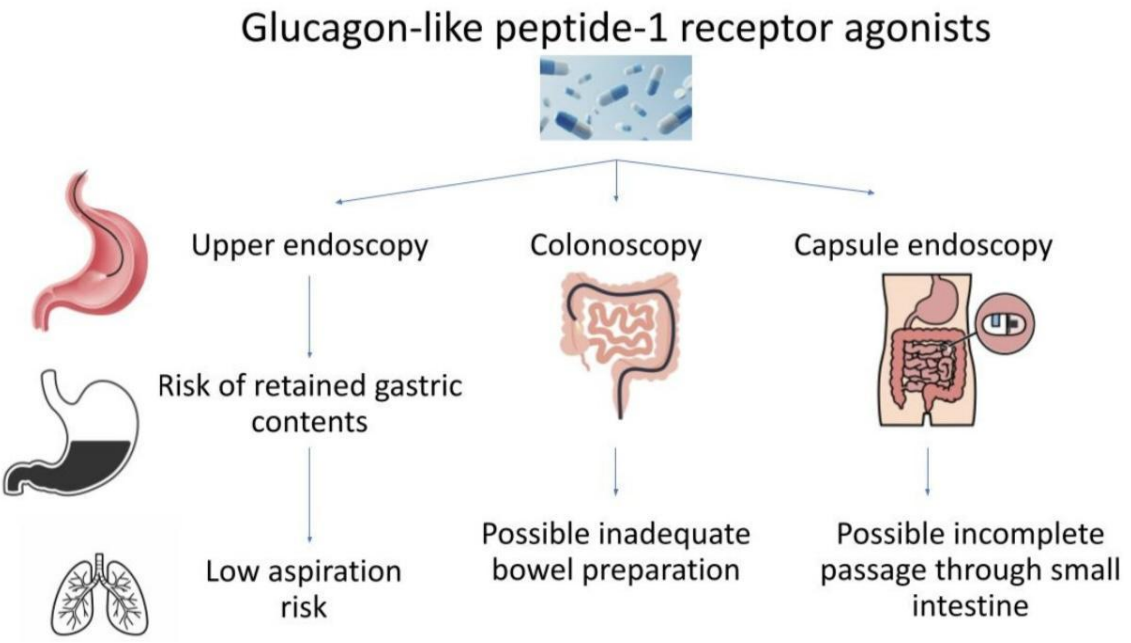

Fig 2. Impact of GLP-1 RAs on endoscopy [10].

The physiological basis and anesthetic implications of these observations have been explored in narrative reviews, such as those by Crowley et al. and Milder (2024). The report shows how GLP-1RAs, thanks to their incretin-mimicking properties, affect gastrointestinal movement and stomach capacity, causing liquids and solids to remain in the stomach longer [5]. These effects use complicated neurohormonal pathways, and aren't just from feeling full, they can increase when combined with opioids or sedatives [7]. As anesthetics, these drugs change stomach function, possibly increasing the chance of inhaling stomach contents, affecting how airways are managed, and making it necessary to rethink the criteria for swiftly inserting a breathing tube [4]. These effects are important for the drugs' weight-loss benefits, but the reviews stress they're also crucial for perioperative safety [5].

Mechanistically, GLP-1RAs have a direct effect on vagal nerve activity, increasing afferent vagal signals and decreasing gastric motility. Due to this vagally mediated effect, gastric emptying is slower and gastric retention times are longer, notably in the proximal stomach [5]. Delayed gastric emptying gets even worse thanks to hormones' effects on stomach muscles and reduced antral contractions, causing food to stay longer [7]. The reasons for retained gastric material despite following typical fasting protocols are these vagal and hormonal processes, which are the physiological foundation for existing anesthetic anxieties [4].

Anesthetic and Aspiration Risks

Clinically relevant cases of aspiration and reflux have been reported in patients using GLP-1 agonists undergoing surgery, despite prolonged fasting [5][11]. Occasionally, airway procedures and surgical preparations have found solid or particulate gastric contents, requiring immediate anesthetic adjustments [11]. Bronchial aspiration has been seen in

some cases without obvious preoperative gastric problems, suggesting that GLP-1RA inhibitors may cause occult gastric stasis [5][10]. Perioperative audits from multiple centers show more aspiration problems in GLP-1RA users than in non-users [4][9].

Clinical experience of anesthesiologists shows that GLP-1RA therapy makes airway management significantly unpredictable [5][11]. Ultrasound detection of a “full stomach” during induction has led to immediate modifications to the anesthesia plan: rapid sequence induction, repositioning the patient, or postponing the procedure (see Table 1 [5][6]. Last-minute modifications can prolong the anesthesia preparation period, increasing stress and causing delays in the operating room [1][2]. Some facilities have instituted preoperative screening procedures for those taking GLP-1RA inhibitors, in an attempt to find at-risk patients before surgery; however, aspiration is still possible despite these efforts [3][4].

The risk of aspiration is particularly high during gastrointestinal procedures, where the airway may be compromised [9][11]. Reviews of gastrointestinal endoscopy in the World Journal show that retained solids in the stomach can make upper endoscopic visualization very difficult, increase the need for aspiration, and make the procedure take longer [9]. Anesthesia combined with undetected gastric contents can significantly increase the risk of aspiration when instruments are used or moved [11]. Preoperative screening is recommended To ensure fasting hours, assess the stomach and other routine procedures [4][9].

Current International Guidelines

Among the most important recommendations for the management of patients taking GLP-1 receptor antagonists before, during, and after surgery are the 2023 AAP consensus statement, which addressed both elective and urgent cases [2][9][12]. Suggestions included discontinuing daily medications on the day of surgery and weekly medications a week before, as well as checking patients' stomachs on the day of surgery [12]. If discontinuation of medications is not possible in an emergency setting, the AAP suggested treating the patient as if they had a "full stomach" and modifying anesthesia, such as using rapid sequence induction and airway protection [2].

During the 2023-2025 period, the AAP, the American Association of Gastroenterological Pathology (AAGBI), and Gastroenterology, among others, issued various guidelines on the use of GLP-1 receptor antagonists [13][14][15][16]. Some guidelines support the Advertising Standards Agency (ASA) rule of discontinuing weekly medication for one week, while others prefer a personalized approach that takes into account each patient's risks, procedure, and clinical setting [13][14]. Some UK advice favors preoperative gastric ultrasound to guide anaesthesia in high-risk patients, rather than discontinuing all medication [15]. The range in these guidelines indicates the uncertainty in balancing the risk of aspiration from delayed gastric emptying with the metabolic risks of discontinuing GLP-1RA treatment [16].

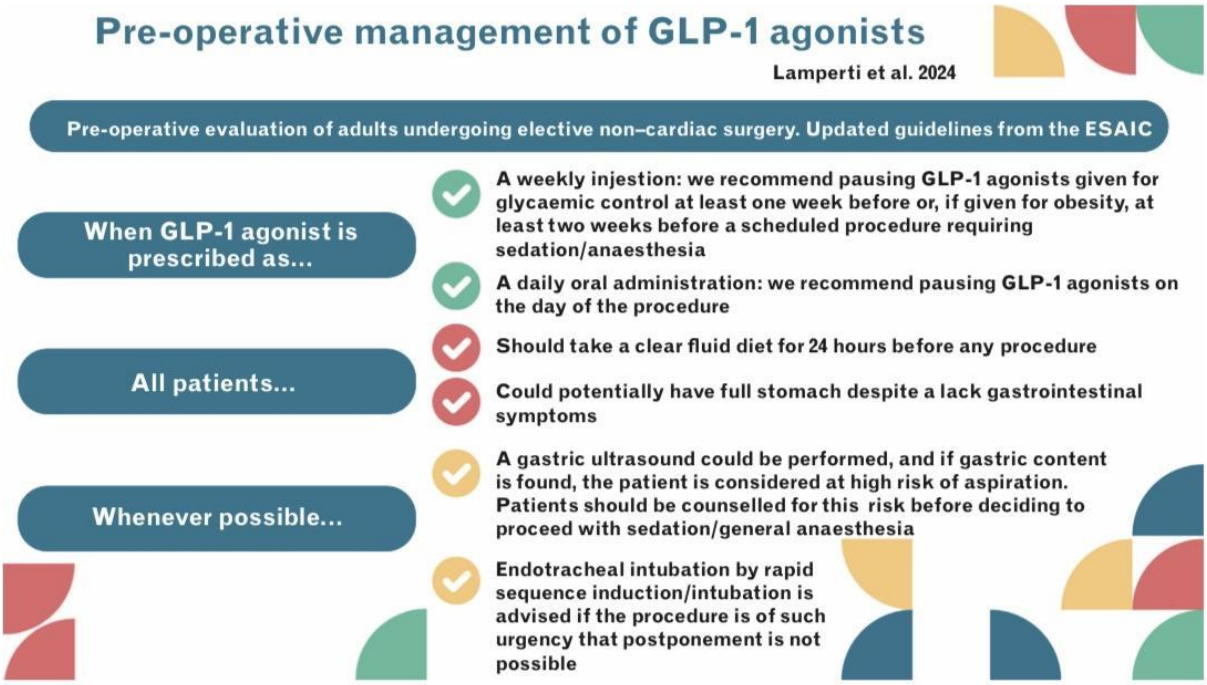

Fig 3.Preoperative management of glucagon-like-peptide-1 agonists [15].

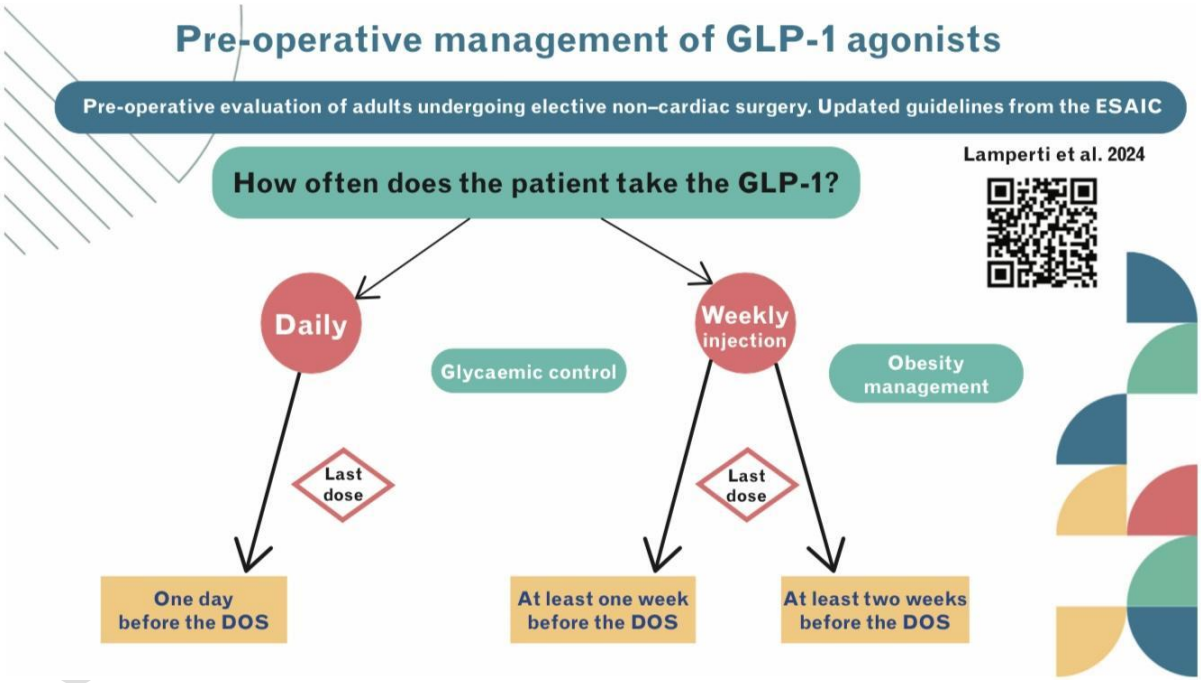

Fig 4. Schematic diagram of preoperative management of glucagon-like-peptide-1 agonists [15].

Current guidelines, supported by multiple medical organizations, indicate that discontinuation of GLP-1 receptor antagonists (GLP-1RAs) such as tirzepatide (Mounjaro) prior to surgery may not always be necessary, particularly for patients without major risk factors for slow

gastric emptying [1][14][17][18][19]. However, in certain patients, particularly those on maintenance therapy without significant gastrointestinal complications, treatment may be continued with some modifications, such as a clear liquid diet for 24 hours prior to surgery to limit gastric contents [19]. For patients with diabetes or heart failure, this strategy prevents metabolic problems with the use of diet and airway protection for aspiration therapy [14][17].

Variables and risk factors				Outcomes
Drug	**Patient**	**Procedure**	**Anaesthesia**	
Drug	Indication	Urgency	Technique	Pulmonary aspiration
Dose	Co-morbidities	Nature	Airway	Glycaemic control
Route	Other drugs			Weight gain
Commencement	Fasting status			Complications of rapid sequence intubation

Table 3. Variables and risk factors, as well as potential outcomes, that need to be considered with respect to peri-operative GLP -1 receptor agonist management [17].

CONCLUSION

Tirzepatide, a dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 receptor agonist (GLP-1RA), offers superior glycemic and weight control compared to monotherapy agents. However, its pharmacodynamic effects on gastric emptying present significant perioperative concerns, particularly regarding aspiration risk. Emerging evidence indicates that delayed gastric emptying may persist despite adherence to standard fasting guidelines, necessitating revised anesthetic protocols.

In Saudi Arabia, where GLP-1RA use is increasing amid high obesity prevalence, these implications are particularly relevant. Current international recommendations vary, with some advocating for preoperative discontinuation and others supporting individualized assessment using gastric ultrasound. Given the metabolic risks associated with abrupt cessation, anesthesiologists must balance glycemic stability against aspiration risk, especially in urgent or high-risk surgical contexts.

Further research is warranted to establish evidence-based fasting durations, validate point-of-care gastric assessment tools, and develop stratified perioperative risk models. Until such data are available, context-specific protocols—integrating local epidemiology, clinical resources, and multidisciplinary input—are essential to optimize perioperative safety in patients receiving Tirzepatide.

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