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Clinical Practice Recommendations regarding patients taking GLP-1 receptor agonists and dual GLP-1/GIP receptor co-agonists prior to anaesthesia or sedation for surgical and endoscopic procedures.

A consensus clinical practice recommendation endorsed by the Australian Diabetes Society (ADS), National Association of Clinical Obesity Services (NACOS), Gastroenterological Society of Australia (GESA) and Australian and New Zealand College of Anaesthetists (ANZCA).

Purpose of this document

To provide recommendations for managing patients taking glucagon-like peptide-1 receptor agonists (GLP-1RAs) and dual GLP-1/glucose-dependent insulintrophic peptide receptor co-agonists (GLP-1/GIPRAs) prior to anaesthesia or sedation for surgical and endoscopic procedures.

Scope

This advice applies to all practitioners providing moderate to deep procedural sedation or anaesthesia. Although focused on surgical and endoscopic procedures, the principles should apply to any procedures requiring anaesthesia or sedation.

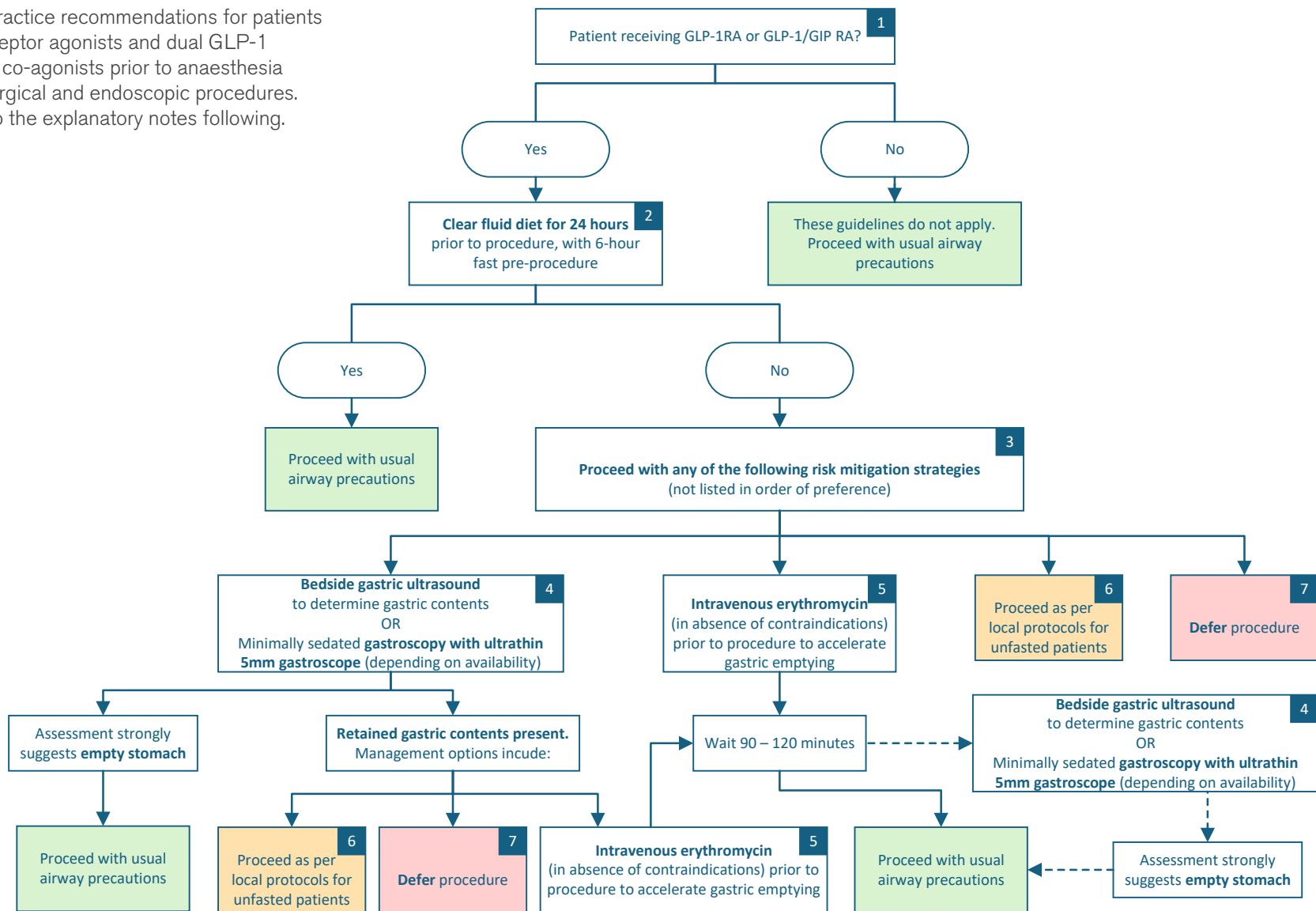
Background

In response to case reports and large case series of retained gastric contents and pulmonary aspiration during sedation for endoscopic procedures or general anaesthesia in people with diabetes and/or obesity treated with GLP-1RAs or GLP-1/GIPRAs, a clinical practice recommendation regarding the periprocedural use of GLP-1RAs and GLP-1/GIPRAs has been co-authored and updated by representatives from ADS, NACOS, GESA and ANZCA. The below represents a consensus based on review of currently available evidence and expert opinion. Although the current level of evidence remains limited, new data and other multidisciplinary clinical guidelines [1, 2] have been considered. This document was written to mitigate the risk of pulmonary aspiration with the periprocedural use of GLP-1RAs and GLP-1/GIPRAs which, although rare, is high-risk and potentially fatal.

Recommendations relating to GLP-1RAs and GLP-1/GIPRAs and sedation or anaesthesia:

- All patients should be asked about the use of GLP-1RAs and GLP-1/GIPRAs prior to anaesthesia or sedation for surgical and endoscopic procedures and be involved in discussion and planning regarding the risk of aspiration.
- Elective preprocedural cessation of GLP-1RAs and GLP-1/GIPRAs is not recommended, and risks hyperglycaemia in people with diabetes and may compromise weight control where patients are taking GLP-1RAs and GLP-1/GIPRAs for this indication.
- Patients should be asked about the use of other medications and medical conditions which may exacerbate gastrointestinal symptoms and delay gastric emptying, such as, but not limited to bowel dysmotility, gastroparesis, and Parkinson's disease.
- Preprocedural diet modification with 24-hour clear fluid diet, followed by standard 6-hour fasting, should be recommended for all patients receiving GLP-1 RAs and GLP-1/GIPRAs.
- Risk mitigation options should be undertaken for those who have not withheld solids for 24 hours. These include detection of residual gastric contents, prokinetic agents, modification of anaesthesia, or deferral of procedure (see figure and explanatory notes).

Figure: Clinical practice recommendations for patients taking GLP-1 receptor agonists and dual GLP-1 and GIP receptor co-agonists prior to anaesthesia or sedation for surgical and endoscopic procedures. Numbers relate to the explanatory notes following.



Explanatory notes

1. Patients should be asked about the use of GLP-1RA and GLP-1/GIPRAs prior to undergoing anaesthesia or sedation.

The patient, prescribing clinician, proceduralist or surgeon and the anaesthetist should be involved with discussions regarding planning for the procedure, including risks and benefits of withholding therapy and those of alternative and mitigating strategies [2].

a. Elective preprocedural cessation of GLP-1RA and GLP-1/GIPRAs is not recommended.

Currently, there are insufficient data to support the cessation of GLP-1RA and GLP-1/GIPRAs prior to anaesthesia [2]. Omission of longer-acting GLP-1RA and GLP-1/GIPRAs for 1-2 weeks is unlikely to alter gastric emptying. Omission for an extended duration may delay urgent surgery or lead to poor glycaemic control at the time of surgery with consequent risks of increased morbidity, length of stay and potentially further deceleration of gastric emptying resulting from hyperglycaemia. Substitution of a different class of glucose-lowering drug for several weeks is often very challenging. Omission of therapy for prolonged periods may compromise weight control where patients are taking GLP-1RAs and GLP-1/GIPRAs for this indication.

It is also recommended that GLP-1RAs with a shorter half-life (i.e. liraglutide) be continued. In individual circumstances, withholding liraglutide for 3 to 4 days may be considered, however, this may have implications for glycaemic control and weight management. There is no current evidence to support any added safety benefits of this practice.

The duration of inhibition of gastric emptying from longer acting GLP-1RA and GLP-1/GIPRAs is unknown and may potentially be several weeks. It has been widely assumed that longer-acting GLP-1RAs do not slow gastric emptying with sustained administration because of tachyphylaxis. This assumption is not supported by existing evidence. The three longer-acting GLP-1RAs that have been assessed using scintigraphy, the 'gold-standard' method for quantifying gastric emptying - liraglutide [3-5], exenatide QW [6] and semaglutide sc (1.0 mg/wk) [7] – have been shown to slow gastric emptying with sustained administration of 8 – 16 weeks duration. Further studies, using appropriate methods, to characterise the effect of long-term administration of longer-acting GLP-1RAs and GLP-1/GIPRAs on gastric emptying are a priority.

b. Absence of symptoms is an unreliable indicator of gastric emptying

The relationship between upper gastrointestinal symptoms (nausea and vomiting) and slowing of gastric emptying by GLP-1RAs is weak. The majority of studies that have evaluated the relationship between the effects of GLP-1RAs on gastric emptying and gastrointestinal symptoms in health, obesity, or T2D found no or low correlations [8-10]. A recent retrospective study of 404 patients undergoing elective oesophagogastroduodenoscopy found an association of semaglutide use with both the presence of preoperative digestive symptoms (nausea/vomiting, dyspepsia, abdominal distension) and residual gastric content, however numbers were small [11]. Based on these limited data, the presence of gastrointestinal side effects is not a reliable indicator of the degree of slowing of gastric emptying.

c. Incidental interruption of therapy

Given possible supply issues, GLP-1RA and GLP-1/GIPRA therapy may have been interrupted due to lack of availability. If GLP-1RA and GLP-1/GIPRA therapy has been interrupted for 4 elimination half-lives or more (see Table 1) it may be assumed that the effect of the medication on gastric emptying is no longer present.

Table 1: GLP-1 RAs and Dual GLP-1 and GIP co-agonists registered for use in Australia

Agent	Receptor agonism	Elimination half-life	Administration schedule	Trade name
Liraglutide	GLP-1	12.6 – 14.3 hours	Once daily	Victoza (up to 1.8 mg) Saxenda (up to 3.0 mg)
Dulaglutide	GLP-1	4.7 – 5.5 days	Once weekly	Trulicity
Semaglutide	GLP-1	5.7 – 6.7 days	Once weekly	Ozempic (up to 1 mg) Wegovy (up to 2.4 mg)
Tirzepatide	GLP-1 & GIP	4.2 – 6.1 days	Once weekly	Mounjaro

2. A 24-hour clear liquid diet may help empty gastric contents.

Two recent systematic reviews and meta-analyses found an increased risk of retained gastric contents at oesophagogastroduodenoscopy in continuous GLP-1RA users compared with controls. In contrast, the rate of retained gastric contents in GLP-1RA users undergoing both oesophagogastroduodenoscopy and colonoscopy was significantly reduced [12, 13]. This suggests that a 24-hour clear liquid diet prior to GI endoscopy may mitigate the risk of retained gastric contents without discontinuing GLP-1RA therapy.

The composition of what constitutes a liquid diet varies amongst centres and is also the basis of ongoing studies. Although conservative, a 'clear liquids' diet, as advised in preoperative fasting guidelines, is considered the most appropriate option at this time. Local practice recommendations for clear liquids diet form the best guide at this stage. The ADS-ANZCA Perioperative Diabetes and Hyperglycaemia Guidelines (Adults) provides further information and guidance regarding the management of diabetes medications during this period.

Prior to the procedure, recommended fasting guidelines should be followed from 6 hours (see ANZCA Professional Document PG07 Preanaesthesia consultation Appendix 1).

3. Residual gastric contents are likely in patients taking GLP-1RAs and may increase aspiration risk. Risk mitigation strategies are necessary.

A number of case reports and small case series of retained gastric contents at the time of gastroscopy or anaesthesia, in people with diabetes and/or obesity treated with GLP-1 RAs, have been published [11, 14-20]. These reports suggest that GLP-1 RAs pose a threat to periprocedural patients, by increasing the risk of pulmonary aspiration of regurgitated gastric contents. To date, there have been 6 case reports of pulmonary aspiration at the time of endoscopy or anaesthesia in patients treated with GLP-1RAs [11, 16, 19, 20]. A large population-based, retrospective cohort study using a health insurance database (including ~800,000 patients undergoing endoscopy) found a higher incidence of aspiration pneumonia (0.83% vs 0.63%) in GLP-1RA users compared to non-users, associated with a significantly higher risk of aspiration pneumonia (hazard ratio 1.33; 95% confidence interval 1.02–1.74; $p=0.036$). When subgrouped by endoscopy type, the risk appeared to be associated with upper endoscopy, combined upper and lower endoscopy but not lower endoscopy alone [21]. Retrospective case-control studies of patients undergoing upper gastrointestinal endoscopy have found a 4- to 10-fold increase in the frequency of residual gastric contents with GLP-1RA use compared with controls [11, 15, 22]. Although only anecdotal, case reports found that retained gastric contents were present despite appropriate fasting, of 8 hours for clear fluids to 20 hours for solids [17]. A small prospective observational study of overnight fasted healthy volunteers, 10 of whom were taking semaglutide for weight management and 10 controls who were not taking semaglutide, found residual intragastric solids on ultrasound in 90% of semaglutide-treated volunteers compared with 20% of control volunteers. Limitations of this study are that the dose of semaglutide varied from 0.25 – 0.75 mg weekly and the majority of volunteers taking semaglutide had been treated for less than 4 weeks [23]. In contrast, a retrospective study of 1512 individuals taking GLP-1RAs and undergoing oesophagogastroduodenoscopy found retained gastric contents in 9.4%, primarily consisting of solid residue (78.9%) [24]. The limited data on rates of retained gastric contents in people taking GLP-1 RAs are inconsistent.

4. Detection of residual gastric contents may be indicated in some patients

- a. Bedside point of care gastric ultrasound can be used to evaluate gastric content and volume to assess perioperative aspiration risk and guide anaesthetic management. Solid, particulate, or thick fluid content, carrying a high aspiration risk, can be detected based on sonographic appearance [25, 26]. ANZCA Professional Document PG47 Perioperative Diagnostic Point of Care Ultrasound and its accompanying Background Paper provides further information and guidance on training requirements for gastric ultrasound.
- b. Unsedated oesophagogastroduodenoscopy using ultrathin 5–6-mm endoscopes is often well tolerated and allows preservation of airway protective reflexes [27]. Retained gastric contents can be directly visualised. It is important to note that patients may forcibly retch with use of the ultrathin endoscope and oral suction may be required in the event of pharyngeal contamination despite intact protective reflexes. In addition, suction of intra-oesophageal fluid is less efficient with the thinner endoscope.

5. Prokinetic agents such as Erythromycin may accelerate gastric emptying

A single dose of 3mg/kg (up to a dose of 250mg) erythromycin intravenously has been shown to accelerate gastric emptying within 15 minutes [28-35]. In patients with diabetes and gastroparesis a single dose of 200 mg of intravenous erythromycin given 15 minutes prior to starting a meal was able to reduce retained gastric solids from 75% to 22% at 60 minutes and 58% to 6% at 120 minutes compared to baseline [33]. Therefore, we recommend a longer duration of 90-120 minutes between administration of erythromycin and endoscopy when possible. In healthy male subjects receiving a GLP-1 infusion, 200 mg of intravenous erythromycin completely reversed deceleration of gastric emptying whereas other prokinetic drugs including metoclopramide, cisapride and domperidone had no effect [36]. Acute hyperglycaemia has the potential to attenuate the acceleration of gastric emptying by iv erythromycin [37]. Contraindications to the administration of erythromycin should be considered. The effectiveness of intravenous erythromycin to accelerate gastric emptying in individuals on GLP-1RA-based therapy in the periprocedural setting has yet to be evaluated.

Repeat gastric ultrasound may be indicated following the administration of erythromycin, but whilst this may be considered prudent, there is currently no evidence to date to require this (therefore indicated as dotted lines on the flowchart (Figure)).

6. Consider management as for unfasted patients if risk mitigation or delay not possible or desirable.

If a clear fluid diet has not been followed for 24 hours prior to the procedure, all patients taking GLP-1RA and GLP-1/GIPRAs should be considered non-fasted/to have a full stomach. If other risk mitigation strategies are unable to be performed or are unavailable, or concern remains that retained gastric contents are present, anaesthesia should be administered according to local practices for a non-fasted patient. Appropriate anaesthetic techniques should be applied to protect against pulmonary aspiration. Without being prescriptive, consideration should be given to regional anaesthetic techniques with minimal sedation and maintenance of upper airways reflexes, or rapid sequence induction for patients requiring general anaesthesia.

7. Deferral of procedure should be considered if high-risk

If after consideration of the risks and benefits, a decision is made with the patient to defer the procedure, arrangements should be made for the patient to follow a clear fluid diet for 24 hours prior to the rescheduled procedure. Consider a longer period of clear fluid diet if retained gastric contents were present despite following mitigation strategies.

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