Guest Editorial

Perioperative glucagon-like peptide-1 receptor agonists-induced gastroparesis - Is gastric ultrasound the answer?

Submitted: 11-Jun-2024
Revised: 08-Jul-2024
Accepted: 12-Jul-2024
Published: 16-Aug-2024

Suryakumar Narayanasamy, Hari Kalagara[1]
Department of Anesthesiology, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH, [1]Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Jacksonville, FL, USA

Address for correspondence: Dr. Suryakumar Narayanasamy,
Department of Anesthesiology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, MLC 2001, Cincinnati - 45229-3039, USA.
E-mail: Suryakumar.Narayanasamy@cchmc.org

Access this article online

Website: https://journals.lww.com/ijaweb

DOI: 10.4103/ija.ija_609_24

Quick response code

INTRODUCTION

Glucagon-like peptide-1 (GLP-1) is a hormone that belongs to the incretin family secreted by the intestinal tract during feeding, which enhances insulin secretion, inhibits glucagon secretion in a glucose concentration-dependent manner and delays gastric emptying.[1] GLP-1 receptor agonists (RAs) exert their glucose-lowering effect by stimulating GLP-1 receptors, which have significant glucose-lowering efficacy and the advantage of low incidence of hypoglycaemia. Exenatide (Byetta) and lixisenatide (Lyxumia) are classified as short-acting GLP-1 RAs since the drug's plasma concentration reaches near zero between the doses. Even though liraglutide (Victoza) is dosed once daily, it is classified as a long-acting GLP-1 RA, along with semaglutide (Ozempic, Wegovy) and dulaglutide (Trulicity) due to the constant elevated drug concentrations in between the drug dosages. Multiple studies have shown better glycated haemoglobin (HbA1c) reduction with long-acting GLP-1 RAs than basal insulin injection. They also consistently lead to weight loss as an added benefit.[2,3] Direct comparison of short- versus long-acting GLP-1 RAs showed that long-acting GLP-1 RAs were better at reducing HbA1c, fasting plasma glucose and body weight and had better gastrointestinal tolerability.[4] GLP-1 RAs have also been shown to significantly reduce major adverse cardiovascular events, which include myocardial infarction, cardiovascular mortality, stroke, all-cause mortality and hospitalisation for heart failure in patients with type 2 diabetes mellitus and preexisting heart disease.[5,6] Nonalcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease in developed countries, which increases the risk of cirrhosis and hepatocellular carcinoma.[7,8] Both semaglutide and liraglutide significantly reduce and reverse biopsy-proven nonalcoholic steatohepatitis (NASH), which is the most severe form of NAFLD.[9,10] This is significant since, currently, there is no United States Food and Drug Administration-approved pharmacological treatment for NASH/NAFLD.[11] In addition to the above indications, GLP-1 RAs are being evaluated for their therapeutic effects on obstructive sleep apnoea, hypertension and polycystic ovarian syndrome.[12-14] Based on the ever-growing on- and off-label indications for GLP-1 RAs, we expect many patients undergoing anaesthesia to be on these medications.

PERIOPERATIVE CONCERNS

GLP-1 RAs can cause significant gastrointestinal side effects such as nausea, vomiting and diarrhoea, in addition to significant gastroparesis. Nausea and

vomiting are more prominent at the initiation of therapy or during dose escalation and tend to subside over time. The mechanism of action is thought to be secondary to centrally mediated action by GLP-1 receptors in the area of postrema.[1] The most significant concern in the perioperative period for anaesthesiologists is the delayed gastric emptying secondary to decreased gastric motility by GLP-1 RAs. In March 2023, Klein and Hobai[15] reported a case of intraoperative pulmonary aspiration in a patient who was on GLP-1 RA (semaglutide). Gulak and Murphy[16] reported another case of regurgitation in a patient who was taking semaglutide. In a small prospective observational study, 90% of healthy volunteers taking semaglutide were found to have solid content in the stomach despite appropriate fasting.[17] Another retrospective observational study showed that fasting patients on semaglutide had a five times higher risk for residual gastric content (RGC) compared to controls.[18] Other retrospective observational studies have shown a 4- to 10-fold increase in RGC in patients taking GLP-1 RAs.[19,20] Most recently, a prospective, cross-sectional study utilising gastric ultrasound found increased RGC at risk for aspiration in 35 of 62 patients on GLP-1 RAs, despite following the standard American Society of Anesthesiologists (ASA) fasting guidelines.[21] The prevalence of increased RGC was greater than 40% even when the GLP-1 RAs were held for 1 week as currently recommended by the ASA expert consensus guidelines.[6] Evidence suggests that continuous stimulation of GLP-1 receptors in healthy volunteers leads to rapid tachyphylaxis of the gastric emptying effect.[22] Short-acting GLP-1 RAs primarily reduce postprandial hyperglycaemia by reducing gastric emptying due to intermittent receptor stimulation. In contrast, long-acting GLP-1 RAs cause a significant effect on gastric emptying at the time of initiation and dose escalation, which might subside over time due to tachyphylaxis.[23-27] So, it is important to consider the type of GLP-1 RA (short versus long acting), dose, indication, duration of treatment, presenting symptoms like abdominal bloating, nausea and vomiting, and recent dose escalation while assessing the risk for delayed gastric emptying in patients on GLP-1 RA medication.

GASTRIC ULTRASOUND

Gastric ultrasound to determine the patients' stomach contents and fasting status has been one of the most useful point-of-care ultrasound (POCUS) applications in perioperative medicine. Until we have large prospective randomised trials with strong evidence, gastric ultrasound could be an excellent bedside diagnostic tool to assess the risk of aspiration by objectively measuring the patient's gastric contents on GLP-1 RAs.

Aspiration is the leading cause of death due to airway-related complications after anaesthesia.[28] ASA closed claims analysis report on pulmonary aspiration found that death was directly associated with pulmonary aspiration in 57% (66/115) of the claims and permanent injury in an additional 14% (16/115) of the claims, and suggests using gastric ultrasound to assess gastric contents for risk assessment.[29]

BASICS

POCUS for assessing RGCs relies on obtaining a satisfactory image of the gastric antrum. This superficial structure underlies the left lobe of the liver, providing a favourable sonographic window. Gastric antrum is a circular structure that distends uniformly in the presence of liquids and/or digested food particles, allowing for a fair estimate of the volume based on previously validated mathematical formulas. Image acquisition is easy to learn and involves placing a low-frequency probe in the parasagittal orientation in the epigastric region in the supine and right lateral decubitus positions.[30-32]

ADVANTAGES

Equipment: Basic ultrasound equipped with a low-frequency probe is universally available in most anaesthesia departments to perform ultrasound-guided nerve blocks.

Image acquisition: Easy to learn with identifiable landmarks such as the liver, aorta and superior mesenteric artery. One study determined that anaesthesiologists need about 33 examinations to achieve a 95% success rate in qualitative bedside gastric ultrasound examinations.[33]

Evidence: There is no robust evidence to support the current ASA expert consensus guidelines for patients on GLP-1 RAs, as more than half of the patients had RGC despite following this guideline in a recent study.[6,21] Gastric ultrasound is the only bedside tool currently available to provide objective evidence of the gastric contents.

Reproducibility (interrater reliability): Ultrasound assessment of antral cross-sectional area is shown to have near-perfect intra- and interrater reliability (correlation coefficient >0.8).[34]

CAUTION

Image acquisition: Inconclusive imaging acquisition can happen in up to 5% of the scans, especially in morbidly obese patients.[35]

False-negative scans: The pyloric sphincter can be mistaken for an empty gastric antrum, leading to the wrong conclusion of an empty stomach. Novice learners need to understand the relationship between the inferior vena cava, aorta, gastric antrum and pyloric sphincter since the consequences of a false-negative report can be catastrophic.

False-positive scans and overdiagnosis: Based on the currently described interpretation of gastric ultrasound images, the presence of air in the stomach leads to the conclusion of a full stomach, even without visualisation of any food particles. This can lead to unnecessary cancellations and invasive airway instrumentations. A few tricks can help minimise the air interference, including placing the patient in the right lateral decubitus position for a few minutes while setting up the machine and interviewing the patient to allow the air to move to the non-dependent part of the stomach (fundus), applying gentle pressure with the probe and tilting the probe to scan towards the body of the stomach to try to look for further evidence of the presence of gastric contents in the presence of air shadow. In a recent study of gastric volume estimation with gastric ultrasound, 19% of control subjects (type 2 diabetes mellitus without GLP-1 RAs) had evidence of RGCs, which is a surprisingly high incidence of a full stomach.[21] Another recent gastric ultrasound study found that the baseline gastric content in fasting diabetics is not higher than that in nondiabetic patients.[36] Interestingly, more than 10% of both populations (11.5% of non-diabetics and 15% of diabetics) had more than 1.5 ml/kg of gastric volume, considered a full stomach under current interpretation guidelines. Most recently, an antral area of 10 cm^2 and a volume threshold of 2.3 ml/kg were identified as the 95th percentile cut-off for fasting individuals.[37] Hundreds of thousands of patients following the standard fasting guidelines undergo general anaesthesia every day without clinically significant aspiration. These findings rekindle the age-old question of 'How much is too much?', especially in the era of encouraging liberal fluid intake, and beg the question, 'Is it time to consider placing less emphasis on a specific volume threshold for clear liquids and more emphasis on the presence of solid materials?'[38]

Inconclusive image: Excessive bowel gas in the colon (air interference), the presence of a gastric tube and prior abdominal surgeries can alter the anatomy, leading to the inability to visualise the stomach with the ultrasound.

CONCLUSION

With sufficient training and expertise, point-of-care gastric ultrasound can quickly assess residual gastric content in the perioperative period in patients on Glucagon-like peptide-1 receptor antagonists.

ORCID

Hari Kalagara: https://orcid.org/0000-0002-2037-032X
Suryakumar Narayanasamy: https://orcid.org/0000-0002-4137-3642

REFERENCES

1. Nauck MA, Quast DR, Wefers J, Meier JJ. GLP-1 receptor agonists in the treatment of type 2 diabetes-state-of-the-art. Mol Metab 2021;46:101102. doi: 10.1016/j.molmet.2020.101102.
2. Singh S, Wright EE Jr, Kwan AYM, Thompson JC, Syed IA, Korol EE, *et al*. Glucagon-like peptide-1 receptor agonists compared with basal insulins for the treatment of type 2 diabetes mellitus: A systematic review and meta-analysis. Diabetes Obes Metab 2017;19:228-38.
3. Abd El Aziz MS, Kahle M, Meier JJ, Nauck MA. A meta-analysis comparing clinical effects of short- or long-acting GLP-1 receptor agonists versus insulin treatment from head-to-head studies in type 2 diabetic patients. Diabetes Obes Metab 2017;19:216-27.
4. Huthmacher JA, Meier JJ, Nauck MA. Efficacy and safety of short- and long-acting glucagon-like peptide 1 receptor agonists on a background of basal insulin in type 2 diabetes: A meta-analysis. Diabetes Care 2020;43:2303-12.
5. Kristensen SL, Rørth R, Jhund PS, Docherty KF, Sattar N, Preiss D, *et al*. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: A systematic review and meta-analysis of cardiovascular outcome trials. Lancet Diabetes Endocrinol 2019;7:776-85.
6. Joshi GP, Abdelmalak BB, Weigel WA, Soriano SG, Harbell MW, Kuo CI, *et al*. American Society of Anesthesiologists Consensus-Based Guidance on Preoperative Management of Patients (Adults and Children) on Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists. 2023. Available from: https://www.asahq.org/about-asa/newsroom/news-releases/2023/06/american-society-of-anesthesiologists-consensus-based-guidance-on-preoperative. [Last accessed on 2024 Feb 04].
7. Harrison SA, Gawrieh S, Roberts K, Lisanti CJ, Schwope RB, Cebe KM, *et al*. Prospective evaluation of the prevalence of non-alcoholic fatty liver disease and steatohepatitis in a large middle-aged US cohort. J Hepatol 2021;75:284-91.

8. Younossi ZM, Golabi P, de Avila L, Paik JM, Srishord M, Fukui N, *et al*. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: A systematic review and meta-analysis. J Hepatol 2019;71:793-801.
9. Armstrong MJ, Gaunt P, Aithal GP, Barton D, Hull D, Parker R, *et al*. Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): A multicentre, double-blind, randomised, placebo-controlled phase 2 study. Lancet 2016;387:679-90.
10. Newsome PN, Buchholtz K, Cusi K, Linder M, Okanoue T, Ratziu V, *et al*. A placebo-controlled trial of subcutaneous semaglutide in nonalcoholic steatohepatitis. N Engl J Med 2021;384:1113-24.
11. Patel Chavez C, Cusi K, Kadiyala S. The emerging role of glucagon-like peptide-1 receptor agonists in managing NAFLD. J Clin Endocrinol Metab 2022;107:29-38.
12. Hamilton GS, Edwards BA. The potential impact of GLP-1 agonists on obstructive sleep apnoea. Respirology 2023;28:824-5.
13. Blackman A, Foster GD, Zammit G, Rosenberg R, Aronne L, Wadden T, *et al*. Effect of liraglutide 3.0 mg in individuals with obesity and moderate or severe obstructive sleep apnea: The SCALE Sleep Apnea randomised clinical trial. Int J Obes (Lond) 2016;40:1310-9.
14. Yazıcı D, Yapıcı Eser H, Kıyıcı S, Sancak S, Sezer H, Uygur M, *et al*. Clinical impact of glucagon-like peptide-1 receptor analogs on the complications of obesity. Obes Facts 2023;16:149-63.
15. Klein SR, Hobai IA. Semaglutide, delayed gastric emptying, and intraoperative pulmonary aspiration: A case report. Can J Anaesth 2023;70:1394-6.
16. Gulak MA, Murphy P. Regurgitation under anesthesia in a fasted patient prescribed semaglutide for weight loss: A case report. Can J Anaesth 2023;70:1397-400.
17. Sherwin M, Hamburger J, Katz D, DeMaria S. Influence of semaglutide use on the presence of residual gastric solids on gastric ultrasound: A prospective observational study in volunteers without obesity recently started on semaglutide. Can J Anesth 2023;70:1300-6.
18. Silveira SQ, da Silva LM, de Campos Vieira Abib A, de Moura DTH, de Moura EGH, Santos LB, *et al*. Relationship between perioperative semaglutide use and residual gastric content: A retrospective analysis of patients undergoing elective upper endoscopy. J Clin Anesth 2023;87:111091. doi: 10.1016/j.jclinane.2023.111091.
19. Stark JE, Cole JL, Ghazarian RN, Klass MJ. Impact of glucagon-like peptide-1 receptor agonists (GLP-1RA) on food content during esophagogastroduodenoscopy (EGD). Ann Pharmacother 2022;56:922-6.
20. Kobori T, Onishi Y, Yoshida Y, Tahara T, Kikuchi T, Kubota T, *et al*. Association of glucagon-like peptide-1 receptor agonist treatment with gastric residue in an esophagogastroduodenoscopy. J Diabetes Investig 2023;14:767-73.
21. Sen S, Potnuru PP, Hernandez N, Goehl C, Praestholm C, Sridhar S, *et al*. Glucagon-like peptide-1 receptor agonist use and residual gastric content before anesthesia. JAMA Surg 2024;159:660-7.
22. Nauck MA, Kemmeries G, Holst JJ, Meier JJ. Rapid tachyphylaxis of the glucagon-like peptide 1-induced deceleration of gastric emptying in humans. Diabetes 2011;60:1561-5.
23. Meier JJ, Menge BA, Schenker N, Erdmann S, Kahle-Stephan M, Schliess F, *et al*. Effects of sequential treatment with lixisenatide, insulin glargine, or their combination on meal-related glycaemic excursions, insulin and glucagon secretion, and gastric emptying in patients with type 2 diabetes. Diabetes Obes Metab 2020;22:599-611.
24. Meier JJ, Rosenstock J, Hincelin-Méry A, Roy-Duval C, Delfolie A, Coester H-V, *et al*. Contrasting effects of lixisenatide and liraglutide on postprandial glycemic control, gastric emptying, and safety parameters in patients with type 2 diabetes on optimized insulin glargine with or without metformin: A randomized, open-label trial. Diabetes Care 2015;38:1263-73.
25. Drucker DJ, Buse JB, Taylor K, Kendall DM, Trautmann M, Zhuang D, *et al*. Exenatide once weekly versus twice daily for the treatment of type 2 diabetes: A randomised, open-label, non-inferiority study. Lancet 2008;372:1240-50.
26. Umapathysivam MM, Lee MY, Jones KL, Annink CE, Cousins CE, Trahair LG, *et al*. Comparative effects of prolonged and intermittent stimulation of the glucagon-like peptide 1 receptor on gastric emptying and glycemia. Diabetes 2014;63:785-90.
27. Jelsing J, Vrang N, Hansen G, Raun K, Tang-Christensen M, Knudsen LB. Liraglutide: Short-lived effect on gastric emptying -- long lasting effects on body weight. Diabetes Obes Metab 2012;14:531-8.
28. Cook TM, Woodall N, Frerk C. Major complications of airway management in the UK: Results of the fourth national audit project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 1: Anaesthesia†. Br J Anaesth 2011;106:617-31.
29. Warner MA, Meyerhoff KL, Warner ME, Posner KL, Stephens L, Domino KB. Pulmonary aspiration of gastric contents: A closed claims analysis. Anesthesiology 2021;135:284-91.
30. Perlas A, Chan Vincent WS, Lupu Catalin M, Mitsakakis N, Hanbidge A. Ultrasound assessment of gastric content and volume. Anesthesiology 2009;111:82-9.
31. Perlas A, Van de Putte P, Van Houwe P, Chan VWS. I-AIM framework for point-of-care gastric ultrasound. Br J Anaesth 2015;116:7-11.
32. Van de Putte P, Perlas A. Ultrasound assessment of gastric content and volume. Br J Anaesth 2014;113:12-22.
33. Arzola C, Carvalho JC, Cubillos J, Ye XY, Perlas A. Anesthesiologists' learning curves for bedside qualitative ultrasound assessment of gastric content: A cohort study. Can J Anaesth 2013;60:771-9.
34. Kruisselbrink R, Arzola C, Endersby R, Tse C, Chan V, Perlas A. Intra- and interrater reliability of ultrasound assessment of gastric volume. Anesthesiology 2014;121:46-51.
35. Van de Putte P, Perlas A. Gastric sonography in the severely obese surgical patient: A feasibility study. Anesth Analg 2014;119:1105-10.
36. Perlas A, Xiao MZX, Tomlinson G, Jacob B, Abdullah S, Kruisselbrink R, *et al*. Baseline gastric volume in fasting diabetic patients is not higher than that in nondiabetic patients: A cross-sectional noninferiority study. Anesthesiology 2024;140:648-56.
37. Perlas A, Arzola C, Portela N, Mitsakakis N, Hayawi L, Van de Putte P. Gastric volume and antral area in the fasting state: A meta-analysis of individual patient data. Anesthesiology 2024;140:991-1001.
38. Van de Putte P, Perlas A. The link between gastric volume and aspiration risk. In search of the Holy Grail? Anaesthesia 2018;73:274-9.

How to cite this article: Narayanasamy S, Kalagara H. Perioperative glucagon-like peptide-1 receptor agonists–induced gastroparesis – Is gastric ultrasound the answer? Indian J Anaesth 2024;68:746-9.