

EDITORIAL

Coming full circle: could glucagon-like peptide-1 receptor agonists confer a net perioperative benefit?

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Summary

Despite a clear association with an increased incidence of unsuspected full stomach presentations, and the release of numerous societal guidelines recommending caution, the relation between glucagon-like peptide-1 receptor agonist (GLP-1RA) use and periprocedural pulmonary aspiration is debatable. Several large retrospective studies (with serious limitations) have found risk either slightly increased or, more commonly, unchanged, compared with non-users. Completing these findings, a new observational study demonstrates a substantial inverse relation, in association with improvement in mortality, cardiovascular risk, and a host of other outcomes. These surprising and fortunate findings recall a multitude of recently demonstrated beneficial effects of GLP-1RA therapy in nonsurgical patients, and reveals a complex, potentially bidirectional relationship between GLP-1RA use and the risk of periprocedural aspiration.

Keywords: diabetes mellitus; gastroparesis; glucagon-like peptide 1 receptor agonists; pneumonia; pulmonary aspiration; postoperative outcomes

The way in which the anaesthesia community has perceived incretin-based therapies such as glucagon-like peptide-1 receptor agonists (GLP-1RAs) and GLP-1RA/glucose-dependent insulinotropic polypeptide (GIP) (here grouped as GLP-1RA) has had a convoluted trajectory. At first, there was optimism. In a series of studies, administration of one or few doses of GLP-1RA immediately before major surgery or in critically ill patients was shown to improve glycaemic control and decrease insulin requirements.¹ Although these effects were not associated with improvement in the incidence of hypoglycaemia, cardiovascular complications, or mortality, these findings were received with enthusiasm.

Then, concerns arose. In March 2023, three publications^{2–4} (including a case report from one of us) alerted the anaesthesia community about the potential danger of unsuspected full stomach presentations associated with GLP-1RA use. Since then, a host of studies have validated this concern, both retrospectively in endoscopy patients and prospectively, using point-of-care gastric ultrasound examinations in surgical patients and volunteers.⁵ Without exception, GLP-1RA users showed a higher incidence of fasting full stomach presentations than control patients, with a risk four to 10 times higher. In many cases, depending on definitions and methodology, 30–50% of fasting patients taking GLP-1RAs presented for elective procedures with full stomachs.^{6,7}

How do these findings align with previous results? And why has this become apparent now, when this drug class has been available for >15 yr and there has not been a significant safety

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signal for pulmonary aspiration during that time? A recent review on the gastrointestinal effects of GLP-1RAs⁸ showed that the majority of clinical trials looking at the effect on gastric emptying were done on people using the older, shorter-acting agents (which are no longer used), or with individuals who were generally fit and well, or in patients on the drugs just a short time. There are almost no studies looking at people with type 2 diabetes mellitus who have been on the newer, weekly agents (with demonstrated cardiovascular safety) for sufficient time for tachyphylaxis to have developed. This is the cohort most likely to have an anaesthetic procedure.

For the 80 yr since Curtis Mendelson published his seminal research, we have known that it is dangerous to anaesthetise patients with full stomachs. Because of that, a series of additional precautionary measures have been recommended by professional societies of anaesthesiologists from the USA, Canada, Europe, Australia, and New Zealand. In general, these measures aimed to either (1) normalise the incidence of fasting full stomach presentations by preoperative withholding of GLP-1RAs or an extended nil-per-os (NPO) period; (2) identify patients at risk on the day of surgery by gastric ultrasound; or (3) prevent pulmonary aspiration even in 'full stomach' patients. Collectively called 'full stomach precautions', the latter measures include performing cases under conscious sedation with or without regional anaesthesia (i.e. 'awake') or with rapid sequence induction of general with tracheal intubation. Most importantly, explicitly or implicitly, all recommendations advised increased vigilance.

Do glucagon-like peptide-1 receptor agonists increase the risk of pulmonary aspiration?

However, not all were convinced that these additional precautions were necessary. The important question was: *in the absence of any additional precautions* (this obvious condition is essential, as we will discuss later), is the incidence of perioperative pulmonary aspiration actually increased in patients taking GLP-1RAs? With a baseline incidence of three in 10 000 cases, early single-centre retrospective studies^{9,10} did not achieve the necessary power. This is when a new, exciting, and unprecedented (at least for the study of pulmonary aspiration) approach appeared, taking advantage of the availability of large commercial patient databases with data collected from millions of cases in the USA. Pharmacoepidemiologists could then search these databases for specific terms and, for example, determine the incidence of documented perioperative pulmonary aspiration in cohorts of hundreds of thousands of patients taking GLP-1RAs. Using this approach in patients undergoing endoscopy, two studies^{11,12} that compared GLP-1RA users with non-users found a small but significant increase in the incidence of pulmonary aspiration. Three other studies^{13–15} that used an 'active comparator' approach (and compared GLP-1RA users with users of dipeptidyl peptidase-4 inhibitors, sodium-glucose co-transporter 2 inhibitors, or with remote GLP-1RA users) found the rate of aspiration to be unchanged. In surgical patients, four studies that compared GLP-1RA users with non-users, again, found no difference in the incidence of pulmonary aspiration.^{16–19}

However, some serious limitations were soon recognised in these studies. Although this approach allowed many cases to be examined, the granularity of observations was low. For example, GLP-1RA users were defined as patients with an active prescription, without knowing whether they took the drug or not before the operation, and if not, for how long they

held it. The number of cases that were cancelled because of a suspected full stomach was also unknown, and, most importantly, the type of anaesthesia used was, in the best case, unknown, and in the worst case, of a nature that could be reasonably expected to minimise (if not erase) any differences that might have been associated with GLP-1RA use. For example, studies of endoscopy (with the exception of Alkabani and colleagues¹⁵) pooled together patients managed with propofol-induced deep sedation (i.e. at risk for aspiration) with those managed with conscious sedation or general anaesthesia with tracheal intubation (which represent, at least partially, 'full stomach precautions'). In studies in surgical patients, the situation was even more perplexing: all four studies enrolled specifically patients managed with general anaesthesia with tracheal intubation. One of them¹⁷ included surgical cases that came directly from the emergency room to the operating room, in patients who most likely did not fast and were likely managed with 'full stomach precautions' anyway, whether they used GLP-1RAs or not. These data do not support the risk aspiration in these patients as being a significant issue, but the fact that the incidence of aspiration was not increased in patients taking GLP-1RAs and managed with full stomach precautions does not deny a potential association in the absence of these measures. As such, none of the studies (with one exception¹⁵) really answered the question they aimed to address, and we still do not have sufficient evidence to help us determine whether the incidence of pulmonary aspiration is increased in patients taking GLP-1RAs, in the absence of any of the recommended additional precautions. This absence of data was highlighted in the UK by the publication of a multidisciplinary consensus document stating that GLP-1RAs should not be stopped in the perioperative period.²⁰

New findings showing reduced risk of pulmonary aspiration

The study by Wu and colleagues²¹ published in the current issue of the *British Journal of Anaesthesia* follows the same strategy, but does not fall into this error. The authors repeatedly emphasise that they know that they studied a 'real-world cohort, involving anti-aspiration measures of unknown prevalence' and refrain from making unwarranted speculations on their necessity. While avoiding drawing unsubstantiated conclusions, they uncovered a most remarkable finding: not only that the risk of pulmonary aspiration was not increased in people with diabetes mellitus on GLP-1RAs compared with non-users, but also that the risk was actually greatly decreased, to 25–30% of that in non-users. All-cause mortality (relative risk [RR]: 0.38), and the incidence of major adverse cardiovascular events (MACEs; RR: 0.58) and acute kidney injury (RR: 0.54), was also decreased. Other postoperative complications, such as diabetic ketoacidosis (RR: 0.25), urinary tract infection (RR: 0.70), sepsis (RR: 0.43), surgical site infection (RR: 0.58), haemorrhage (RR: 0.63), and delirium (RR: 0.36), were also better in the GLP-1RA cohort. These findings were robust and held true across several subgroup analyses. Although the inverse association was observed for all GLP-1RAs users, the protective effect was stronger for those who started GLP-1RA >90 days before surgery, which suggests these are direct drug effects, not confounders.

Several limitations inherent to their approach are fully acknowledged by the authors. This was an observational study, derivation of the main outcome and confounders from

International Classification of Diseases (ICD) codes makes them vulnerable to misclassification, and many unmeasured factors remain, such as to what extent ‘GLP-1RA prescription holders’ actually used the drug, held it before surgery, and adhered to the extended fasting recommendations. The anaesthetic technique used is also unknown, as is the duration and complications of diabetes mellitus, etc. Moreover, many of the secondary outcomes reported (sepsis, delirium, etc.) were not prespecified, and not only should be seen as hypothesis-generating only, but also increase the risk of false-positives.

With these caveats, the findings of Wu and colleagues²¹ are not to be underestimated. At first, they might appear surprising. One can agree that ‘full stomach’ measures might prevent an increase in the incidence of pulmonary aspiration in ‘full stomach’ patients, but an actual decrease is something else altogether. Could it be possible that, because of our increased awareness, patients taking GLP-1RAs have been managed with ‘aspiration precautions’, which leads to a partial prevention of the baseline incidence of aspiration? Another, more speculative interpretation (which is favoured by the authors) brings into discussion a host of general beneficial effects of GLP-1RAs. In nonsurgical patients with diabetes mellitus, GLP-1RAs have been associated with decreased all-cause and cardiovascular mortality, decreased incidence of myocardial infarction and stroke, and a slowed progression of kidney disease.²² In surgical patients, a host of postoperative complications appear to be reduced in GLP-1RA users compared with non-users, such as rates of hospital re-admission, wound dehiscence, and others.^{23,24} Some of these findings could be explained by improved glycaemic control and weight loss, but others could not, and recall a host of other beneficial effects of GLP-1RAs demonstrated so far only in animal experimental studies. Among these are preconditioning, antiinflammatory and anti-reperfusion effects.²⁵ As such, the current study by Wu and colleagues²¹ would not be the first that reports beneficial effects associated with GLP-1RA use, but with unclear and speculative mechanisms.

Why was this inverse relationship not seen in previous studies?^{16–19} One (unlikely) possibility was that it is variable, and the (yet unknown) underlying mechanisms might be present in some patients²¹ but not in others.^{16–19} Given the multifactorial, systemic nature of the mechanisms postulated, it is difficult to see how this could be so. Another possibility that cannot be ignored is that GLP-1RAs might exert opposite effects on the incidence of pulmonary aspiration: a systemic, protective effect (demonstrated in the current study) and a causative effect, as a result of the increased incidence of full stomach presentations, and it is the latter that is variable. As mentioned, previous studies used shorter-acting agents, often in healthy people or those with diabetes mellitus taking the drugs for relatively short periods of time, and thus were not representative of the general surgical population on these agents. Because the prevalence and efficiency of full stomach precautions are the main unknown parameters in these studies, this is perhaps easier to accept. It is therefore equally possible that in previous studies,^{16–19} the decrease in aspiration incidence seen here was nullified by a simultaneous increase, itself being the result of unmitigated full stomach presentations. In other words, the demonstration of a net protective effect in this study²¹ might force us to postulate a balancing causative effect in previous studies^{16–19} to account for the net equivalent result. This is all speculative, of course, and perhaps other possibilities exist.

Nevertheless, the data presented by Wu and colleagues²¹ are to be welcomed. We may be coming full circle. Before the aspiration concerns were recognised, many endocrinologists started initiating GLP-1RA therapy before surgery in patients with diabetes mellitus or obesity, hoping for improved post-operative outcomes. This trend was subsequently reversed, and we specifically recommended delaying starting GLP-1RAs until after impending surgery. Now, if the improvement in operative outcomes demonstrated by Wu and colleagues²¹ proves reproducible, and we become more confident that we can either normalise the incidence of full stomach presentations in patients taking GLP-1RAs or prevent their sequelae, we might consider reverting to the original strategy, and expect an improvement in a host of perioperative outcomes. While more surprises may be waiting ahead, the future looks exciting.

Declarations of interest

KD declares honoraria, travel fees for speaking, or being on advisory boards from Abbott Diabetes, AstraZeneca, Boehringer-Ingelheim, Eli Lilly, Menarini, Novo Nordisk, Roche, and Sanofi Diabetes. The other authors declare that they have no conflicts of interest.

References

- Hulst AH, Plummer MP, Hollmann MW, et al. Systematic review of incretin therapy during peri-operative and intensive care. *Crit Care* 2018; 22: 299
- Klein SR, Hobai IA. Semaglutide, delayed gastric emptying, and intraoperative pulmonary aspiration: a case report. *Can J Anaesth* 2023; 70: 1394–6
- Kobori T, Onishi Y, Yoshida Y, et al. Association of glucagon-like peptide-1 receptor agonist treatment with gastric residue in an esophagogastroduodenoscopy. *J Diabetes Invest* 2023; 14: 767–73
- Silveira SQ, da Silva LM, de Campos Vieira Abib A, 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
- Oprea AD, Umpierrez GE, Sweitzer B, Hepner DL. Perioperative management of patients taking glucagon-like peptide-1 receptor agonists: applying evidence to clinical practice. *Anesthesiology* 2024; 141: 1141–61
- Nersessian RSF, da Silva LM, Carvalho MAS, et al. Relationship between residual gastric content and perioperative semaglutide use assessed by gastric ultrasound: a prospective observational study. *Anaesthesia* 2024; 79: 1317–24
- Sen S, Potnuru PP, Hernandez N, et al. Glucagon-like peptide-1 receptor agonist use and residual gastric content before anesthesia. *JAMA Surg* 2024; 159: 660–7
- Jalleh RJ, Rayner CK, Hausken T, Jones KL, Camilleri M, Horowitz M. Gastrointestinal effects of GLP-1 receptor agonists: mechanisms, management, and future directions. *Lancet Gastroenterol Hepatol* 2024; 9: 957–64
- Anazco D, Fansa S, Hurtado MD, Camilleri M, Acosta A. Low incidence of pulmonary aspiration during upper endoscopy in patients prescribed a glucagon-like peptide 1 receptor agonist. *Clin Gastroenterol Hepatol* 2024; 22: 1333–5
- Milne AD, Berry MA, Ellis MW, Dobson GR. Rates of glucagon-like peptide-1 receptor agonist use and

- aspiration events associated with anesthesia at a Canadian academic teaching centre. *Can J Anaesth* 2024; **71**: 673–5
11. Yeo YH, Gaddam S, Ng WH, et al. Increased risk of aspiration pneumonia associated with endoscopic procedures among patients with glucagon-like peptide 1 receptor agonist use. *Gastroenterology* 2024; **167**: 402. 4.e3
 12. Al Sakka Amini R, Ismail AS, Al-Aqrabawi M, et al. Risk of aspiration pneumonitis after elective esophagogastroduodenoscopy in patients on glucagon-like peptide-1 receptor agonists. *Cureus* 2024; **16**, e66311
 13. Barlowe TS, Anderson C, Sandler RS, et al. Glucagon-like peptide-1 receptor agonists do not increase aspiration during upper endoscopy in patients with diabetes. *Clin Gastroenterol Hepatol* 2025; **23**: 739–47
 14. Peng CY, Chang YC, Gong C, et al. Association between glucagon-like peptide-1 receptor agonists and aspiration pneumonia during endoscopic procedures. *Anesthesiology* 2024; **141**: 1009–12
 15. Alkabbani W, Suissa K, Gu KD, et al. Glucagon-like peptide-1 receptor agonists before upper gastrointestinal endoscopy and risk of pulmonary aspiration or discontinuation of procedure: cohort study. *BMJ* 2024; **387**, e080340
 16. Klonoff DC, Kim SH, Galindo RJ, et al. Risks of peri- and postoperative complications with glucagon-like peptide-1 receptor agonists. *Diabetes Obes Metab* 2024; **26**: 3128–36
 17. Dixit AA, Bateman BT, Hawn MT, Odden MC, Sun EC. Preoperative GLP-1 receptor agonist use and risk of postoperative respiratory complications. *JAMA* 2024; **331**: 1672–3
 18. Chen YH, Zink T, Chen YW, et al. Postoperative aspiration pneumonia among adults using GLP-1 receptor agonists. *JAMA Netw Open* 2025; **8**, e250081
 19. Poeran J, Iban YC, Zhong H, et al. Preoperative GLP-1 agonist use is not associated with perioperative aspiration or pneumonia: an observational study using US national data. *Br J Anaesth* 2025; **134**: 1526–8
 20. El-Boghdadly K, Dhesi J, Fabb P, et al. Elective peri-operative management of adults taking glucagon-like peptide-1 receptor agonists, glucose-dependent insulinotropic peptide agonists and sodium-glucose cotransporter-2 inhibitors: a multidisciplinary consensus statement: a consensus statement from the Association of Anaesthetists, Association of British Clinical Diabetologists, British Obesity and Metabolic Surgery Society, Centre for Perioperative Care, Joint British Diabetes Societies for Inpatient Care, Royal College of Anaesthetists, Society for Obesity and Bariatric Anaesthesia and UK Clinical Pharmacy Association. *Anaesthesia* 2025; **80**: 412–24
 21. Wu H-L, Chen J-T, Cata JP, Hsieh C-H, Cherng Y-G, Tai Y-H. Risk of perioperative cardiorespiratory complications and mortality associated with preoperative glucagon-like peptide-1 receptor agonist use in type 2 diabetes mellitus: a nationwide propensity-score matched study. *Br J Anaesth* 2026; **136**: 86–97
 22. Nong K, Jeppesen BT, Shi Q, et al. Medications for adults with type 2 diabetes: a living systematic review and network meta-analysis. *BMJ* 2025; **390**, e083039
 23. Aschen SZ, Zhang A, O'Connell GM, et al. Association of perioperative glucagon-like peptide-1 receptor agonist use and postoperative outcomes. *Ann Surg* 2025; **281**: 600–7
 24. Kamarajah SK, Gudionzi N, Findlay JM, Lee MJ, Pinkney T, Markar SR. Evaluation of safety of preoperative GLP-1 receptor agonists in patients undergoing elective surgery: a systematic review, meta-analysis and meta-regression. *EClinicalMedicine* 2025; **87**, 103408
 25. Ravassa S, Zudaire A, Diez J. GLP-1 and cardioprotection: from bench to bedside. *Cardiovasc Res* 2012; **94**: 316–23