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GLP-1 receptor agonist use does not increase risk of respiratory complications post-endoscopy

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Supplementary Material is available at https://doi.org/10.1055/a-2487-2937

Key words
Quality and logistical aspects, Performance and complications, Preparation, Endoscopy Upper GI Tract, Endoscopy Lower GI Tract

received 21.10.2024
accepted after revision 21.11.2024
accepted manuscript online 25.11.2024

Bibliography
Endosc Int Open 2025; 13: a24872937
DOI 10.1055/a-2487-2937
ISSN 2364-3722

Georg Thieme Verlag KG, Oswald-Hesse-Straße 50, 70469 Stuttgart, Germany

ABSTRACT

Background and study aims Data on respiratory complications associated with GLP-1 receptor agonist (GLP-1 RA) use before endoscopic procedures are limited.

Patients and methods We conducted a retrospective cohort study using TriNetX in adults with diabetes or obesity on GLP-1 RAs within 3 months of endoscopy, comparing them with non-GLP-1 RA users. Propensity score matching and Cox proportional hazards models were used to assess outcomes.

Results Among 46,948 patients, no significant differences in post-endoscopy aspiration pneumonitis (hazard ratio [HR] 0.92, 95% confidence interval [CI] 0.54–1.56) or pneumonia (HR 1.01, 95% CI 0.83–1.24) were found between groups.

Conclusions GLP-1 RA use before endoscopy does not increase respiratory complications, supporting continued preoperative medication use.

Introduction

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are approved for diabetes treatment and recently, for weight loss, potentially addressing the global obesity epidemic, metabolic syndrome, and cardiovascular risk [1]. GLP-1 RAs are incretin mimics that prompt glucose-dependent insulin release from the pancreatic islets, reducing glucagon secretion, increasing satiety, and delaying gastric emptying [2].

In September 2023, the American Gastroenterological Association (AGA) addressed management of patients taking GLP-1 RAs, finding no evidence to support all patients stopping GLP-1 RAs before elective endoscopy procedures [3]. This was in response to the American Society of Anesthesiologists recommendation to discontinue GLP-1 RAs before elective procedures [4] due to reports suggesting an increased risk of aspiration and respiratory complications in patients who present for procedures requiring sedation [5,6]. Although preoperative medication guidelines can prevent complications, withholding medications can result in adverse effects and significant logistical burdens, including procedure cancellations, care delays, and financial losses [7,8]. These issues are particularly significant for GLP-1 RAs, which require withholding periods of up to a week. Consequently, the ASA preoperative suggestions may

necessitate enhanced nursing resources, exacerbating barriers and care delays for patients requiring endoscopic procedures [3]. Furthermore, it may not be appropriate to withhold these medications, given the clear benefit of GLP-1 RAs in cardiovascular health and glycemic control in diabetic patients, and it is unclear if withholding a single dose is sufficient for gastric motility to return to normal. We conducted a real-world analysis to determine risk of respiratory complications in patients prescribed GLP-1 RAs within 3 months of an endoscopic procedure.

Patients and methods

We conducted a population-based retrospective cohort study using TriNetX, a global federated health research network with anonymized electronic medical records from 83 large healthcare organizations. We included all patients aged 18 to 70 years with type 2 diabetes mellitus or overweight/obesity with active GLP-1 RA prescriptions within 3 months before undergoing endoscopic procedures defined by current procedural terminology codes. The age cutoff was set at 70 years to minimize confounding from age-related comorbidities and the higher baseline risk of pneumonia in older adults. The study period ranged from January 1, 2018, to December 31, 2022. For the GLP-1 procedure cohort, we selected patients who underwent endoscopic procedures during the study period and who had an active GLP-1 RA prescription within 3 months before the procedure. For the control group, we selected patients who had endoscopic procedures between January 01, 2018, and June 30, 2022, and who had never received a GLP-1 prescription in their entire lifetime. The control group enrollment period was shortened by 6 months to ensure that the sample size remained within the TriNetX processing capacity. Patients with a history of surgery, anesthesia, or mechanical ventilation within 3 months before the procedure were excluded.

The primary outcome was aspiration pneumonitis or pneumonia within 30 days of endoscopic procedures in patients taking preoperative GLP-1 RAs. Secondary outcomes included risk association of other outcomes, per procedure, and individual GLP-1 RA. The study was deemed exempt by the institutional review board and is reported in accordance with the STROBE guidelines [9].

We performed 1:1 propensity score matching using patient demographics, Charlson comorbidity index, aspiration risk factors, and frailty risk (**Supplementary Table 1**). We used Kaplan-Meier analysis and log-rank tests on the TriNetX platform to compare the time to event for all outcomes between cohorts. GLP-1RA users were 1:1 matched to non-users using the Greedy algorithm. A standardized mean difference below 0.1 between characteristics after matching was deemed appropriate. We calculated the association of aspiration using risk ratio and hazard ratio (HR), with 95% confidence intervals (CIs) from a univariate Cox proportional hazards model. The proportionality of hazards was checked with scaled Schoenfeld residuals. For outcomes not meeting the proportional hazards assumption, we conducted a landmark analysis at 3 months. To explore potential unknown confounders, we performed an E-value sensitivity analysis for HR and CI using an online tool. Statistical significance was set at 0.05.

Results

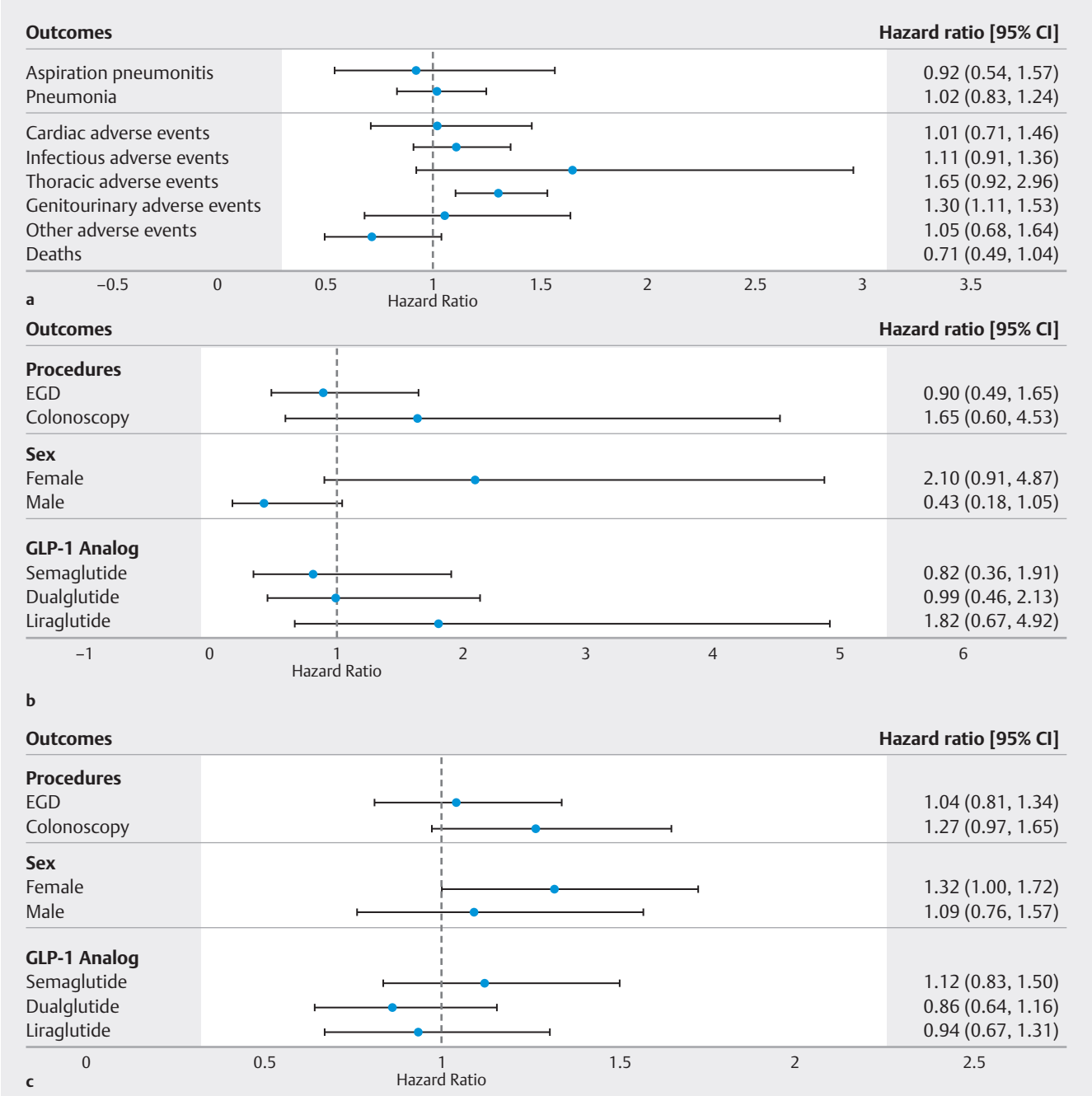
Of the 1,018,770 patients undergoing endoscopy, 29,094 were prescribed GLP-1 RAs and 989,676 were not. Of these, 46,948 patients met inclusion criteria, 23,474 in the GLP-1 RA cohort and 23,474 in the comparison group with baseline demographics shown in Table 1. As shown in ▶ **Fig. 1a**, overall incidence of post-endoscopy aspiration pneumonitis was 0.11% for those with GLP-1 RA prescriptions and 0.12% for those without (HR 0.92; 95% CI 0.54–1.56; P = 0.752). Similarly, incidence of pneumonia was not significantly different between those with GLP-1 RA prescription (0.81%) and those without (0.79%) (HR 1.01; 95% CI 0.83–1.24; P = 0.877). Risk of other adverse events (AEs) post-endoscopy was also not significantly different between these two groups. On subgroup analysis, there was no significant difference between incidence of aspiration pneumonitis or pneumonia for the type of endoscopic procedure or specific GLP-1 RA (▶ **Fig. 1b**, ▶ **Fig. 1c**, ▶ **Table 1**). CIs were wide for aspiration pneumonitis but narrow for pneumonia and subgroup analysis. There was no significant difference in the Charlson comorbidity index, risk factors for aspiration, and frailty between the groups.

Discussion

GLP-1 RA use before endoscopy was not associated with a higher risk of post-procedure respiratory complications compared with that in patients not prescribed GLP-1 RAs. In our subgroup analysis by procedure, gender, and GLP-1 RA medication, this was also the case. Previous studies have indicated that use of GLP-1 RAs is associated with retained gastric contents, which is a direct consequence of delayed gastric emptying [5]. The clinical impact of solid and liquid gastric emptying is different. Retained contents in the stomach may not pose a significant issue for patients undergoing combined esophagogastroduodenoscopy and colonoscopy, because they typically fast and consume only a liquid diet the day before the procedures and do not consume solids during that time. Given that our study included more participants undergoing colonoscopy than EGD, duration of fasting may have contributed to our findings of no increased risk of respiratory complications.

Although the nationwide rate of aspiration is reported to be around 1%, our findings indicated a lower rate. This may be due to the participants undergoing colonoscopy. The lower aspiration rate may also be attributed to differences in patient management practices across multiple hospitals and lack of standardized protocols that exists in our population-based study that includes data from numerous healthcare organizations. In addition, it is possible that not all aspirations may have been reported, because they may not have been clinically significant or accurately documented. This could lead to underestimation of the true incidence of respiratory complications.

Our study has certain limitations. We were unable to measure preoperative duration of GLP-1 RA therapy, duration of fast-



▶ **Fig. 1** Incidence of aspiration pneumonitis and pneumonia among GLP-1 RA users and non-users post-endoscopy. **a** Incidence of respiratory complications and other adverse events post-upper and/or lower endoscopy. **b** Results of subgroup analysis of incidence of aspiration pneumonitis stratified by endoscopy type, sex, and GLP-1 RA. **c** Subgroup analysis of incidence of pneumonia stratified by endoscopy type, sex, and GLP-1 RA.

ing, medication adherence, or cessation of medication before endoscopic procedures. Our selection of the 2018 to 2022 cohort was made before concerns arose regarding risk of aspiration associated with GLP-1 RAs. Our study did not measure gastric contents; however, previous studies have addressed the association between GLP-1 RA use and retained gastric contents [5]. This retrospective study relies on accurate documentation of symptoms, disease, and treatments, rendering it susceptible to biases in charting, coding, and recall. Our study has wide CIs, which may be due to low incidence of these events and a larger series is needed to further address the incidence and impact of GLP-1 RAs in this setting.

Our results align with those of Dixit et al. (2024), who found that use of GLP-1 RAs before emergency surgery did not increase risk of respiratory complications [10]. However, Yeo et al. (2024) reported an increased risk of aspiration pneumonia

▶ **Table 1** Baseline characteristics and risk of adverse events post-endoscopy in GLP-1 RA users and non-users: Subgroup analysis of aspiration pneumonitis and pneumonia risk by procedure type, sex, and GLP-1 RA.

Outcomes	GLP-1 cohort	Control cohort	Hazard ratio (95% CI)	*P* value
Sample size before match	29,094	989,676	NA	NA
Sample size after match	23,474	23,474	NA	NA
Age	53.8 ± 9.3 years	54.2 ± 10.0 years	NA	NA
Females	58.7%	59.2%	NA	NA
Males	36.1%	35.5%	NA	NA
White	60.1%	59.3%	NA	NA
African American	19.3%	20.4%	NA	NA
Hispanic	10.6%	10.7%	NA	NA
Diabetes mellitus	76.1%	78.7%	NA	NA
Overweight BMI and obesity	67.9%	72.3%	NA	NA
Hemoglobin A1c	7.3 ± 2.0	7.1 ± 2.0	NA	NA
BMI	36.1 ± 8.5	35.6 ± 8.9	NA	NA
Post-endoscopy adverse events				
Aspiration pneumonitis	0.11%	0.12%	0.92 (0.54–1.57)	0.752
Pneumonia	0.81%	0.79%	1.01 (0.83–1.24)	0.877
Cardiac adverse events	0.28%	0.28%	1.01 (0.71–1.46)	0.941
Infectious adverse events	0.86%	0.76%	1.11 (0.91–1.36)	0.313
Thoracic adverse events	0.14%	0.08%	1.65 (0.92–0.96)	0.090
Genitourinary adverse events	1.44%	1.10%	1.30 (1.11–1.53)	0.002
Other adverse events	0.19%	0.18%	1.05 (0.68–1.64)	0.819
Deaths	0.20%	0.28%	0.71 (0.49–1.04)	0.076
Subgroup analysis of aspiration pneumonitis				
by procedures				
EGD (n = 11,477)	0.17%	0.19%	0.90 (0.49–1.65)	0.732
Colonoscopy (n = 15,910)	≤ 0.06%	≤ 0.06%	1.65 (0.60–4.53)	0.328
By sex				
Female (n = 13,327)	0.13%	≤ 0.08%	2.10 (0.91–4.87)	0.076
Male (n = 7,893)	≤ 0.13%	0.20%	0.43 (0.18–1.05)	0.056
By GLP medication				
Semaglutide (n = 10,717)	≤ 0.09%	0.11%	0.82 (0.36–1.91)	0.650
Dulaglutide (n = 9,366)	0.14%	0.14%	0.99 (0.46–2.13)	0.976
Liraglutide (n = 6,928)	0.16%	≤ 0.14%	1.82 (0.67–4.92)	0.232
Subgroup analysis of pneumonia				
by procedures				
EGD (n = 11,477)	1.09%	1.04%	1.04 (0.81–1.34)	0.757
Colonoscopy (n = 15,910)	0.78%	0.61%	1.27 (0.97–1.65)	0.081
By sex				
Female (13,327)	0.94%	0.71%	1.32 (1.00–1.72)	0.050
Male (7,893)	0.79%	0.71%	1.09 (0.76–1.57)	0.625

▶ **Table 1** (Continuation)

Outcomes	GLP-1 cohort	Control cohort	Hazard ratio (95% CI)	*P* value
By GLP-1 medication				
Semaglutide (10,717)	0.88%	0.77%	1.12 (0.83–1.50)	0.452
Dulaglutide (n = 9,366)	0.89%	1.01%	0.86 (0.64–1.16)	0.323
Liraglutide (n = 6,928)	0.97%	1.03%	0.94 (0.97–1.31)	0.697

BMI, body mass index; CI, confidence interval; EGD, esophagogastroduodenoscopy; GLP-1, glucagon-like peptide-1 receptor agonists.

associated with GLP-1 RAs following endoscopy [6]. The discrepancy in results might stem from differences in robustness of matching, because some covariates in their study exhibited residual imbalances.

Conclusions

Our study suggests a low incidence of respiratory complications including aspiration post-endoscopy in individuals prescribed a GLP-1 RA. Future large studies are needed to assess respiratory complications post-endoscopy including more complex procedures that require deep sedation, such as endoscopic retrograde cholangiopancreatography or endoscopic ultrasound in which the risk of aspiration could be higher. An individualized approach based on GLP-1 RA indication and symptoms of nausea, vomiting, dyspepsia, or abdominal distention may be the best determinant of who can safely undergo upper and/or lower endoscopy procedures.

Conflict of Interest

The authors declare that they have no conflict of interest.

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