Pre-operative Use of GLP-1 Agonists Does Not Increase the Odds of Aspiration Following Femur Fracture Repair in Adults

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INTRODUCTION: Glucagon-like peptide 1 (GLP-1) receptor agonists are commonly used to treat patients with type 2 diabetes and obesity with at least one weight related comorbidity. GLP-1 agonists exert their main effect by stimulating glucose-dependent insulin release from pancreatic islets; additionally, these drugs have been shown to delay gastric emptying. Delayed gastric emptying is of particular interest in patient optimization for surgery, as patients may have residual gastric content despite preoperative fasting, increasing their risk of aspiration during induction of anesthesia. For patients undergoing elective procedures, GLP-1 agonists can be withheld to mitigate aspiration risk. However, this may not be possible in patients with traumatic injuries requiring timely surgical intervention, such as in the case of proximal femur fractures. It is the standard of care for a repair to occur within 24 hours as this reduces the risk of mortality and other complications in these patients. This study aims to determine the odds of experiencing post-operative aspiration following proximal femur fracture repair (PFFR) in patients who have been prescribed GLP-1 agonists.

METHODS: The TriNetX Research Network was used for data curation and collection. Data queries were executed on 6/16/2025. The data collection window spanned from 5/16/2005 to 5/16/2025 as 1 month of follow up after surgery was required for eligibility. Patients 18 years or older who underwent PFFR within 1 week of receiving inpatient hospital services were included in the overall cohort. Patients were then split into case and control cohorts based on GLP-1 use. Controls had no lifetime use of GLP-1s whereas cases had documented GLP-1 use from the day of surgery back to 1 month prior to surgery. 1:1 propensity matching was then performed accounting for age at surgery, sex, race, ethnicity, and several medical comorbidities and medications (i.e. diabetes mellitus, obesity, Parkinsons disease, multiple sclerosis, gastroparesis, use of opioids or anticholinergics, etc.) that may increase risk for aspiration (Table 1). The main outcome was aspiration defined both individually and collectively by the following International Classification of Diseases (10th edition [ICD-10]) codes: J95, J69.0, J69.8, and T17. Continuous variables are represented by means and standard deviations and are compared using 2-tailed independent samples t-tests. Categorical variables are represented by numbers and percentages and are compared using chi-square or Fisher's exact tests. The "Measures of Association" function in the TriNetX platform was used to perform univariate regressions that generated an odds ratio (OR) and quantified significance. ORs are reported with 95% confidence intervals (95%CI) and a p-value of 0.05 was used as the threshold for statistical significance in all tests.

RESULTS: Of the nearly 150 million potential patients, a total of 137,099 patients met initial inclusion criteria, 636 (0.5%) of which had GLP-1 agonist use within one month of surgery. The other 136,463 (99.5%) patients met inclusion criteria for the control cohort. After propensity matching was performed, 635 patients were included in the case cohort and 635 patients were included in the control cohort for a total of 1,270 subjects. Using all 4 ICD-10 codes for the outcomes, we found that at 1 month after surgery, 20 (3.1%) patients with no GLP-1 use experienced an aspiration event compared to 11 (1.7%) patients with prior GLP-1 use. Patients with a previous history of GLP-1 use as far back as 1 month prior to surgery did not have significantly elevated odds of experiencing an aspiration event up to 1 month after surgery (OR: 1.845; 95%CI: 0.877 – 3.883; p = 0.102). The results of the regression analyses for aspiration using individual ICD-10 codes were also non-significant (see Table 2).

DISCUSSION: The results of our analyses suggest that the odds of aspiration following PFFR are low regardless of recent GLP-1 use and that there is no increased risk of aspiration in patients currently prescribed GLP-1 agonists following PFFR. This finding is contrary to the assumption that delayed gastric emptying observed in patients taking GLP-1 agonists would result in increased aspiration risk. The current literature appears conflicting as to whether GLP-1s increase the risk of aspiration. This is likely due to variability in study design with relation to procedure type and medication formulation. Our findings further contribute to the body of evidence that demonstrates no increased risk of aspiration in patients using GLP-1s. More robust research in this area is required to support or refute our findings.

CLINICAL RELEVANCE: Our findings are unlikely to change the current approach to peri-operative anesthesia management of patients with acute orthopaedic injuries who are also taking GLP-1 agonists. However, our data seems to suggest acute orthopaedic surgery, specifically proximal femur surgery, is not a contraindication in prescribing patients GLP-1 agonists.

Table 1: Results of 1:1 Propensity Matching for Confounding Variables Including Demographics, Comorbidities, and Medications

	Prior to 1:1 Propensity Matching			After 1:1 Propensity Matching		
Variable	**Not Taking GLP-1s**	**Taking GLP-1s**	**p-value**	**Not Taking GLP-1s**	**Taking GLP-1s**	**p-value**
Age at Index (n [mean ± SD])	133,095 (65.2 ± 18.8)	636 (68.9 ± 11.1)	**<0.001**	635 (69.2 ± 12.0)	635 (68.9 ± 11.1)	0.676
Male (n, %)	56,191 (42.2%)	217 (34.1%)	**<0.001**	224 (35.3%)	217 (34.2%)	0.68
Female (n, %)	72,015 (54.1%)	414 (65.1%)	**<0.001**	409 (64.4%)	413 (65.0%)	0.814
White (n, %)	101,309 (76.1%)	512 (80.5%)	**0.01**	519 (81.7%)	512 (80.6%)	0.615
Black or African American (n, %)	13,963 (10.5%)	62 (9.7%)	0.542	62 (9.8%)	61 (9.6%)	0.924
American Indian or Alaska Native (n, %)	388 (0.3%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-
Native Hawaiian or Other Pacific Islander (n, %)	353 (0.3%)	10* (1.6%)	**<0.001**	0 (0.0%)	10* (1.6%)	-
Other Race (n, %)	3,104 (2.3%)	19 (3.0%)	0.275	17 (2.7%)	19 (3.0%)	0.735
Hispanic or Latino (n, %)	7,732 (5.8%)	43 (6.8%)	0.306	38 (6.0%)	43 (6.8%)	0.566
Not Hispanic or Latino (n, %)	100,238 (75.3%)	469 (73.7%)	0.349	468 (73.7%)	469 (73.9%)	0.949
Diabetes mellitus (n, %)	32,834 (24.7%)	576 (90.6%)	**<0.001**	573 (90.2%)	575 (90.6%)	0.849
Overweight and Obesity (n, %)	21,938 (16.5%)	367 (57.7%)	**<0.001**	357 (56.2%)	366 (57.6%)	0.61
Parkinson's Disease (n, %)	4,373 (3.3%)	27 (4.2%)	0.176	24 (3.8%)	27 (4.3%)	0.668
Multiple Sclerosis (n, %)	1,089 (0.8%)	10* (1.6%)	**0.036**	10* (1.6%)	10* (1.6%)	1
Gastroparesis (n, %)	1,500 (1.1%)	22 (3.5)	**<0.001**	18 (2.8%)	22 (3.5%)	0.304
Dysphagia (n, %)	15,155 (11.4%)	92 (14.5%)	**0.015**	85 (13.4%)	92 (14.5%)	0.571
Obstructive Sleep Apnea (n, %)	10,667 (8.0%)	171 (26.9%)	**<0.001**	155 (24.4%)	171 (26.9%)	0.304
Gastroesophageal Reflux Disease (n, %)	37,985 (28.5%)	277 (43.6%)	**<0.001**	270 (42.5%)	276 (43.5)	0.734
Opioids (n, %)	103,527 (77.8%)	560 (88.1%)	**<0.001**	546 (86.0%)	559 (88.0%)	0.278
Anticholinergics (n, %)	16,462 (12.4%)	151 (23.7%)	**<0.001**	148 (23.3%)	150 (23.6%)	0.895

Bolded values indicate statistically significant difference between cohorts.
* To maintain HIPAA compliance, TriNetX uses a minimum value of 10 for each variable if the number of patients categorized by a specific variable is >0 but ≤10.

Table 2: Aspiration events based on ICD-10 codes

ICD-10: J95

Cohort	Patients in Cohort	Patients with Outcome	% Risk	OR	95%CI	p-value
Control	635	13	2.0%	1.306	(0.569, 3.001)	0.528
Case	635	10*	1.6%			

ICD-10: J69.0

Cohort	Patients in Cohort	Patients with Outcome	% Risk	OR	95%CI	p-value
Control	635	10*	1.6%	1.000	(0.413, 2.419)	1.000
Case	635	10*	1.6%			

ICD-10: T17

Cohort	Patients in Cohort	Patients with Outcome	% Risk	OR	95%CI	p-value
Control	635	0	0.0%	-	-	-
Case	635	10*	1.6%			

ICD-10: J69.8

Cohort	Patients in Cohort	Patients with Outcome	% Risk	OR	95%CI	p-value
Control	635	0	0.0%	-	-	-
Case	635	0	0.0%			

ICD-10: J95 or J69.0 or T17 or J69.8

Cohort	Patients in Cohort	Patients with Outcome	% Risk	OR	95%CI	p-value
Control	635	20	3.1%	1.845	(0.877, 3.883)	0.102
Case	635	11	1.7%			

OR = odds ratio, **95%CI** = 95% confidence interval.
* To maintain HIPAA compliance, TriNetX uses a minimum outcome value of 10 if the number of patients who have experienced that outcome is >0 but ≤10.