Evaluating the Association Between GLP-1 RA Prescriptions and New-Onset Dysphagia: *A Population-Based Cohort Study*

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Introduction

- Since their expanded FDA approval for weight loss in 2014, use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) has increased and has been associated with various otolaryngologic side effects.
  - From 2019 to 2022 alone, GLP-1 RA use has almost doubled from 6.3 to 10.4 million Americans.[1]
  - Up to 56% (137.1 million) of Americans are eligible for GLP-1 RA therapy based on current guidelines.[3]
- Initial studies on GLP-1 RAs regarding delayed gastric emptying[4] led to initial perioperative guidelines *restricting their preoperative use*.[5,6]
  - Subsequent meta-analyses do not show significant aspiration risk, reflected in newer guidelines favoring a more personalized approach in determining perioperative risk.[5–9]
  - Their effects on gastric emptying, gastroesophageal reflux, and overall muscle mass loss have raised concerns regarding dysphagia and aspiration.
  - Perioperative guidelines currently recommend temporary discontinuation of these medications prior to general anesthesia.
- However, the association between GLP-1 RAs and dysphagia or aspiration *outside of the perioperative setting* remains unclear

Methods

- This was a propensity-matched cohort analysis of patients with type 2 diabetes mellitus (T2DM) by GLP-1RA prescription status in the TriNetX platform, a federated research platform with aggregated, de-identified electronic health record data of over 130 million patients worldwide.
- The index event was T2DM with GLP-1 RA prescription.
- Propensity score matching was based on age, sex, race, ethnicity, and hyperlipidemia.
- The primary and secondary outcomes were new-onset dysphagia and aspiration pneumonitis within 1 year of the index event, respectively.
- Odds ratios with 95% confidence intervals (CI) were reported.

Results

In TriNetX, 1,381,206 and 8,060,814 T2DM patients with and without GLP-1 RA use were available in the database. Following matching, 382,287 patients were in each propensity-matched cohort.

Table 1. Demographic and Clinical Characteristics Before and After Propensity Matching of Type 2 Diabetes Mellitus Patients in TriNetX by GLP-1 RA Use

	T2DM with GLP-1 RA use N(%)	T2DM without GLP-1 RA use N(%)	P-value
	Before Propensity Matching		
Age at Index	57.7 +/- 13.3	60.9 +/- 15.7	<0.001
Female	764,934 (55.4%)	3,830,675 (49.2%)	<0.001
Race/Ethnicity			
White	893,770 (64.7%)	4,814,925 (61.8%)	<0.001
Hispanic or Latino	137,735 (10.0%)	818,3444 (10.5%)	<0.001
Black or African American	266,398 (19.3%)	1,481,907 (19.0%)	<0.001
Asian	49,034 (3.6%)	380,863 (4.9%)	<0.001
Hyperlipidemia	669,471 (48.5%)	1,036,244. (13.3%)	<0.001
	After Propensity Matching (n=382,287 in each cohort)		
Age at Index	56.8 +/- 13.3	56.8 +/- 13.3	0.95
Female	189,636 (57.8%)	189,644 (57..8%)	0.98
Race/Ethnicity			
White	211,890 (64.5%)	211,923 (64.6%)	0.93
Hispanic or Latino	29,428 (9.0%)	29,400 (9.0%)	0.90
Black or African American	59,777 (18.2%)	59,741 (18.2%)	0.91
Asian	9,812 (3.0%)	14,342 (4.4%)	<0.001
Hyperlipidemia	49,015 (14.9%)	49,010 (14.9%)	0.99

Abbreviation: GLP-1 RA, glucagon like peptide-1 receptor agonist; T2DM, type 2 diabetes mellitus.

- **Dysphagia Events**
  - GLP-1 RA users: 9,311
  - Non-GLP-1 RA users: 11,710s
- **Aspiration Pneumonitis Events**
  - GLP-1 RA users: 1,474
  - Non-GLP-1 RA users: 3,603
- **Primary matched cohort**
  - Dysphagia: **OR 0.79 (0.76-0.81)**
  - Aspiration pneumonitis: **OR 0.41 (0.38-0.43)**
- **Additionally matched for BMI**
  - Dysphagia: **OR 0.9 (0.86-0.95)**
  - Aspiration Pneumonitis: **OR 0.44 (0.40-0.49)**

Discussion & Conclusion

- GLP1 RA prescriptions were associated with lower odds of dysphagia and dysphagia-related events.
- Further research is warranted to elucidate this seemingly protective association with some possible contributory factors below:
  - GLP1-RA use duration
  - Extent of weight loss achieved during GLP-1 RA therapy
  - The role of obstructive sleep apnea, particularly when untreated, and its increased risk of swallowing discoordination and nighttime pulmonary aspiration

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