Risk of Pancreatitis in Obesity Patients: A Retrospective Database Study

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Background and Objective

The risk of gastrointestinal adverse events associated with Glucagon-like peptide-1 (GLP-1) receptor agonists treatment, particularly pancreatitis, has been a subject of ongoing research.[1] Some studies link GLP-1s to higher pancreatitis risk in diabetes patients, while others find no significant difference compared to other medications. However, there remains a gap in real-world evidence on the association between GLP-1 therapy and pancreatitis risk in obesity patients. This retrospective database study aims to address this gap by investigating the incidence of pancreatitis among obesity patients receiving GLP-1 treatment.

Methodology

Data source: Optum® Market Clarity Database

Study Participants

- ≥1 claim or EHR for GLP-1 treatment from July 1, 2015, through December 31, 2023 (index date is the earliest claim or EHR for GLP-1) and ≥1 medical claim with obesity diagnosis code in any position or body mass index (BMI) ≥ 30 kg/m² during the 6-month pre-index period
- At least 6 months of baseline and follow-up continuous enrollment (CE), with no evidence of GLP-1 treatment or pancreatitis during the baseline period
- Obesity patients on GLP-1 treatment were categorized into three cohorts based on the BMI class: Class 1 obesity (30-35 kg/m²), Class 2 obesity (35-40 kg/m²), and Class 3 obesity (BMI ≥40 kg/m²)

Study Measures

- Patient demographics and clinical characteristics, including Charlson Comorbidity Index (CCI) and comorbidities, during the baseline period
- Pancreatitis outcome during the follow-up period

Statistical Methods

- Incidence rates per 100,000 person-years (PY); Kaplan-Meier (KM) analysis to estimate the risk of developing pancreatitis, compared among the obesity classes; all tests were two-sided at α=0.05*
- Sensitivity analysis for comparison of pancreatitis risk among obesity classes, stratified by baseline history of diabetes
- A Cox proportional hazards model was employed to evaluate factors associated with the risk of pancreatitis, adjusting for baseline covariates**

* Statistical testing was performed using exact binomial and log-rank tests
**Covariates included age group, gender, race/ethnicity, region, CCI, baseline comorbidities, and baseline alcohol use and smoking

Results

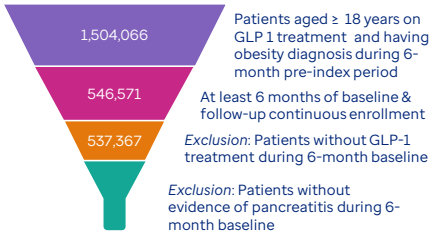

Figure 1. Patient attrition

Demographics		Class 1 Obesity (N=178,633)	Class 2 Obesity (N=141,019)	Class 3 Obesity (N=190,531)
Age	Mean (SD)	54.6 (12.7)	52.7 (12.7)	49.9 (12.7)
Female	%	62.9%	64.3%	68.4%
Commercial only	%	62.2%	63.5%	61.2%
Medicare only	%	23.7%	21.0%	18.4%
Medicaid only	%	13.6%	15.0%	19.9%
Unknown Payor	%	0.5%	0.4%	0.4%
Follow-up time (months)	Mean (SD)	32.7 (25.9)	32.0 (25.7)	31.7 (25.4)
Baseline CCI	Mean (SD)	1.1 (1.5)	1.0 (1.5)	1.0 (1.5)

Table 1. Patient Demographics

Conditions	Class 1 Obesity (N=178,633)	Class 2 Obesity (N=141,019)	Class 3 Obesity (N=190,531)
Type 2 diabetes	59.9%	58.2%	57.4%
Osteoarthritis	16.1%	17.4%	19.7%
Hyperlipidemia	53.5%	49.9%	44.2%
Angina	4.1%	3.5%	2.8%
Dyslipidemia	59.9%	56.2%	50.1%
OSA	16.4%	23.5%	32.6%
CKD	10.6%	9.4%	8.7%
Alcohol use	1.9%	1.6%	1.4%
Smoking	19.8%	19.1%	19.6%

Table 2. Baseline Comorbidities

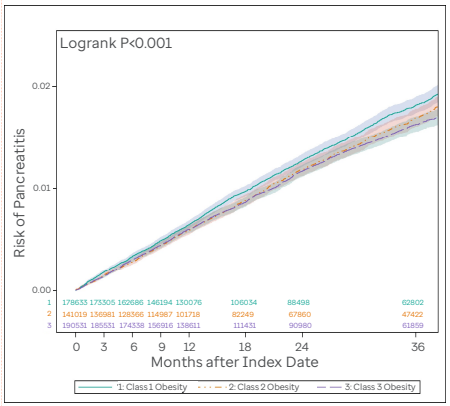

Figure 2. KM Curve – Risk of Pancreatitis among Obesity Classes

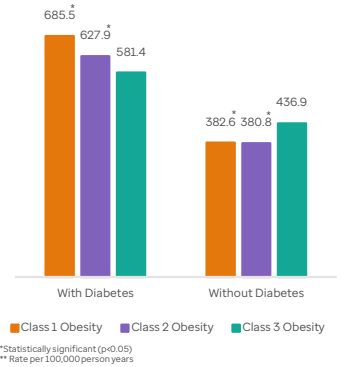

Figure 3. Incidence rates of Pancreatitis among Obesity Classes by Diabetes Status**

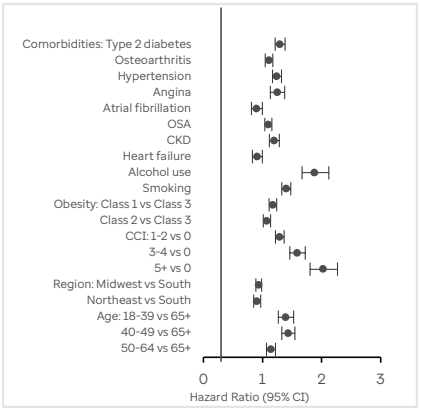

Figure 4. Cox Proportional Hazards Model for Risk of Pancreatitis

- A total of 510,183 adult obese patients with GLP-1 treatment were identified (mean ± SD age: 52.3 ± 12.9 years; follow-up period: 32.1 ± 25.7 months; CCI: 1.0 ± 1.5; 65.3% females; 55.3% Non-Hispanic Whites; 62.2% commercial enrollees).
- The 3-year cumulative incidence rate of pancreatitis in Class 1, Class 2, and Class 3 obesity cohorts was 1.8%, 1.7%, and 1.6%, respectively (p<0.001) (**Figure 2**).
- Diabetes patients with Class 1 and 2 obesity had 17.7% and 7.5% higher pancreatitis incidence than those with Class 3 obesity. Class 3 obesity patients without diabetes had 14.0% and 15.0% higher pancreatitis incidence than those with Class 1 and 2 obesity (**Figure 3**).
- Lower BMI levels, younger age, male sex, higher CCI, history of certain conditions (**Figure 4**), alcohol use, and smoking were associated with increased risk of pancreatitis.

Conclusions

In obese patients on GLP-1 treatment, pancreatitis risk is higher in Class 1 and 2 obesity compared to Class 3, especially in patients with diabetes. Non-diabetic patients with Class 3 obesity show greater risk. Younger age, comorbidities, alcohol use, and smoking increase pancreatitis risk. These findings suggest potential interactions between obesity, diabetes, and pancreatitis risk, possibly indicating a protective role of higher BMI. Future research should explore underlying mechanisms and key factors for better risk prediction and management.

[1]Sodhi M, Rezaeianzadeh R, Kezouh A, Etminan M. Risk of Gastrointestinal Adverse Events Associated With Glucagon-Like Peptide-1 Receptor Agonists for Weight Loss. JAMA. 2023;330(18):1795-1797

Abbreviations: EHR – Electronic health records; CCI – Quan Charlson comorbidity index; COPD - Chronic obstructive pulmonary disease; OSA - Obstructive sleep apnea; CKD - Chronic kidney disease; CI – Confidence interval

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