Health Outcomes and Incidence of Diabetes Among Patients With Severe Hypertriglyceridemia and Acute Pancreatitis

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Purpose

- Patients with severe hypertriglyceridemia (sHTG), in particular triglyceride levels ≥500 mg/dL, are at increased risk for acute pancreatitis (AP).
- Pancreatitis can itself lead to type 2 diabetes mellitus (T2DM), but the strength of this association in patients with sHTG is unknown.
- **We examined the extent to which patients without diabetes with sHTG-AP have an increased incidence of new-onset T2DM compared to similar patients with sHTG alone.**

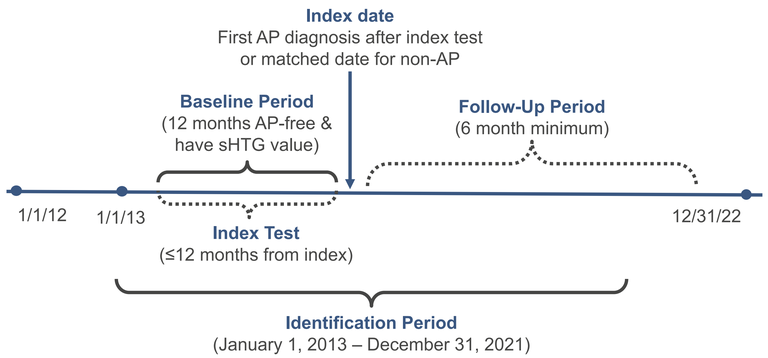
Methods

- Propensity score matched retrospective cohort study in a large, nationally representative healthcare claims database.
- Identified adults without T2DM with sHTG (triglyceride (TG) levels 500-15,000 mg/dL) with AP (ICD-9-CM: 577.0; ICD-10-CM: K85.xx excluding K85.2 and K85.3) between January 2013 - December 2021 and matched them to patients without DM or AP but with sHTG.
- Patients were continuously enrolled 1 year prior to index date (baseline) and were followed for at least 6 months (unless died earlier), either until the end of enrollment or study end (12/31/2022) **(Figure 1)**.

Statistical Analysis

- Propensity score and exact matching used to identify patients with sHTG without AP in a 1:1 ratio.
- Propensity for sHTG-AP estimated with logistic regression including: sociodemographics, insurance, comorbidities, statin and non-statin lipid-lowering medication use, GLP-1 use, index TG value, and total cholesterol. Greedy nearest neighbor method with caliper width of 0.2 of the standard deviation of the logit of the propensity score used for matching.
- Patients matched on index TG value (i.e., 500-879, 880-999, 1000-1999, 2000-15000 mg/dL), and index year. Patients without match were excluded.
- Risk of incident T2DM (≥2 claims with T2DM diagnosis ≥30 days apart) compared between sHTG-AP and sHTG without AP cohorts using Cox regression.

Figure 1. Study Schema



Disclosures
All authors declare the following: support for the present presentation (e.g., funding, provision of study materials, medical writing, etc.): Ionis Pharmaceuticals. **MSB** is an employee of PHAR, which was paid by Ionis Pharmaceuticals to conduct the research described in the abstract. PHAR also discloses financial relationships with the following entities outside of the submitted work: AbbVie, Akcea, Amgen, AstraZeneca, BioMarin Pharmaceuticals, Bristol-Myers Squibb, Boston Scientific Corporation, Eisai, Ethicon, Genentech, Gilead, Novartis, Otsuka, Pfizer, Recordati, Regeneron, Sanofi US Services, Sunovion, Takeda Pharmaceuticals USA. **EC** is an employee of PHAR, which was paid by Ionis Pharmaceuticals to conduct the research described in the abstract. PHAR also discloses financial relationships with the following entities outside of the submitted work: AbbVie, Akcea, Amgen, AstraZeneca, BioMarin Pharmaceuticals, Bristol-Myers Squibb, Boston Scientific Corporation, Eisai, Ethicon, Genentech, Gilead, Novartis, Otsuka, Pfizer, Recordati, Regeneron, Sanofi US Services, Sunovion, Takeda Pharmaceuticals USA. **KFV** reports the following: support for the present abstract: Ionis Pharmaceuticals; KFV is an employee and shareholder of Ionis Pharmaceuticals. **NDW** reports the following: support for present abstract: Ionis Pharmaceuticals; consulting fees: Ionis Pharmaceuticals, Amgen, Novartis, and HeartLung; research support through institution from Regeneron, Novartis, and Novo Nordisk.

Results

At baseline, there were 330 matched pairs of patients with sHTG-AP and sHTG alone without T2DM at baseline **(Table 1)**.

Demographics

- Mean (SD) age of patients with sHTG-AP and sHTG without AP was 51.1 (13.0) and 50.1 (12.6) years, respectively. Both groups had 29.7% (n=98) females.
- Most patients with sHTG-AP and sHTG alone were White, 63.0% (n=208) and 60.9% (n=201), and had commercial health insurance, 73.0% (n=241) and 77.3% (n=255), respectively.

TGs and Other Risk Factors

- Baseline mean (SD) index TG was 1,053.1 (934.4) mg/dL for sHTG-AP and 994.4 (838.2) mg/dL for sHTG without AP.
- Other risk factors, including cholesterol, were similar in both groups at baseline.
- After matching, there were no statistically significant differences in the baseline measure between cohorts (p>0.05).

Table 1. Patient Characteristics at Baseline after Matching

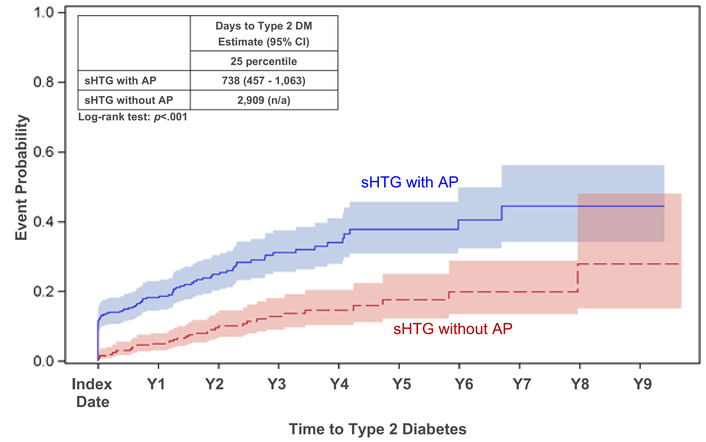
	Matched		
	sHTG-AP	sHTG without AP	p-value
N	330	330	
Age, mean (SD) years	51.1 (13.0)	50.1 (12.6)	0.294
Female, n (%)	98 (29.7)	98 (29.7)	1.000
Race, n (%)			0.669
Asian	14 (4.2)	13 (3.9)	
Black	29 (8.8)	25 (7.6)	
Hispanic	62 (18.8)	77 (23.3)	
White	208 (63.0)	201 (60.9)	
Unknown	17 (5.2)	14 (4.2)	
Years of follow-up, mean (SD)	3.0 (2.2)	2.9 (2.1)	0.876
CCI, mean (SD)	0.9 (1.9)	0.9 (1.7)	0.748
Comorbidities, n (%)			
Atherosclerotic cardiovascular disease	48 (14.5)	46 (13.9)	0.824
Chronic liver disease	47 (14.2)	42 (12.7)	0.569
Chronic kidney disease	20 (6.1)	25 (7.6)	0.440
Disorders of lipoprotein metabolism and other lipidemias*	259 (78.5)	268 (81.2)	0.382
Heart failure	7 (2.1)	6 (1.8)	0.779
Hypertension	188 (57.0)	185 (56.1)	0.814
Obesity	93 (28.2)	83 (25.2)	0.379
Pancreatic necrosis	0 (0)	0 (0.0)	
Persistent organ failure	16 (4.8)	8 (2.4)	0.096
Index TG value (mg/dL), n (SD)	1053.1 (934.4)	994.4 (838.2)	0.396
Total cholesterol value (mg/dL), mean (SD)	264.4 (121.9)	255.8 (105.4)	0.331
Treatments, n (%)			
Lipid-lowering treatment	216 (65.5)	212 (64.2)	0.744
Statins	135 (40.9)	130 (39.4)	0.691
Non-statins	137 (41.5)	151 (45.8)	0.272
PCSK9 inhibitors	2 (0.6)	0 (0.0)	0.499
Fibric acid derivatives	121 (36.7)	123 (37.3)	0.872
GLP-1 agonists and SGLT-2 inhibitors	1 (0.3)	1 (0.3)	1.000
Insurance Type, n (%)			0.207
Commercial	241 (73.0)	255 (77.3)	
Medicare	89 (27.0)	75 (22.7)	

AP=acute pancreatitis; CCI=Charlson comorbidity index; GLP-1=glucagon-like peptide-1
SD=standard deviation; sHTG=severe hypertriglyceridemia; TG=triglycerides
*Does not include hypertriglyceridemia

Follow-up Period

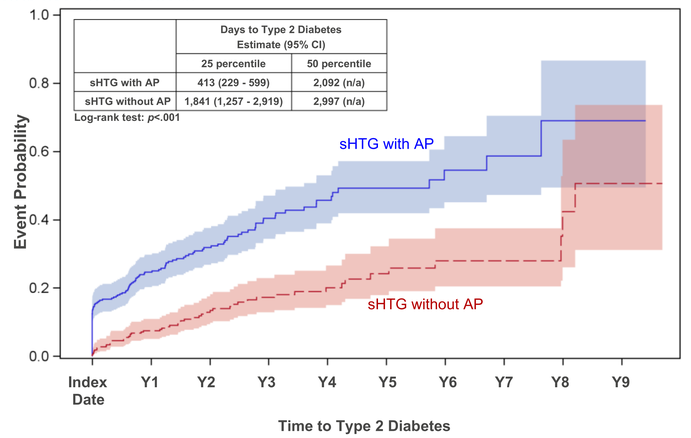
- Mean (SD) follow-up period was 3.0 (2.2) and 2.9 (2.1) years for sHTG-AP and sHTG alone (p=0.876), respectively.
- Incidence of new onset T2DM was 27.9% (n=92) in the sHTG-AP group compared to 11.2% (n=37) in those with sHTG without AP (p <0.001). Risk of T2DM was higher (hazard ratio [95% CI]=2.8 [1.9-4.2]; p <0.001) throughout follow-up in those with sHTG-AP versus with sHTG without AP **(Figure 2)**.
- In a sensitivity analysis (≥1 claim with T2DM), incidence remained higher in patients with sHTG-AP (37.3%, n=123) than in those with sHTG without AP (16.4%, n=54) **(Figure 3)**.

Figure 2. Risk of T2DM* During Follow-up in Matched sHTG Cohorts



*≥2 claims with T2DM diagnosis ≥30 days Apart

Figure 3. Sensitivity Analysis: Risk of T2DM** During Follow-up in Matched sHTG Cohorts



**≥1 claim with T2DM diagnosis

Conclusions

- Among patients with sHTG, **AP is associated with more than double the incidence of new-onset T2DM compared to patients without AP**.
- Preventing initial episodes of AP may have important health benefits, including the reduction of incident diabetes.

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Poster presented at 19th Annual Cardiometabolic Health Congress; Boston, MA; October 17-19, 2024.

This study was funded by Ionis Pharmaceuticals.