Cardiovascular Risk Reduction with GLP-1 RAs in Patients with OSA and Obesity: A Real-World Study

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Background & Objectives

- OSA as an established risk factor for cardiovascular disease.
- GLP-1RAs with potential in reducing CV risk and reducing OSA severity, however, a significant knowledge gap remains on the **impact of GLP-1RAs on CV events in OSA patients**.

→ **Assess the cardiovascular benefits of GLP-1 RAs in OSA patients directly**, rather than relying on risk factors

Method & Study Design

Available patients from
TriNetX Global Collaborative Network Database

Diagnosed for OSA between **Jan 1, 2010, and Dec 1, 2021**

Without history of **acute MI, HF, pulmonary HTN** prior to OSA Diagnosis

Inclusion

Obesity (BMI ≥ 30)

No GLP-1 RAs use at **any time more than 12 months** prior to OSA diagnosis

GLP-1 RA initiated within **12 months** prior to OSA?

Yes / No

EXCLUDE IF: GLP-1 RA initiated after OSA

GLP-1 RA cohort (N=16,990) — Non-GLP-1 RA cohort (N=727,130)

1:1 Propensity Score Matching

GLP-1 RA cohort (N=16,881) — Non-GLP-1 RA cohort (N=16,881)

Follow-up period	3 years from OSA diagnosis (index date)
End point	Survival analysis of new onset acute MI, heart failure, pulmonary hypertension, death from all cause

ICD-10 Code-Based Definitions of Conditions

Condition	ICD-10	Diagnosis
Acute MI	I21	Acute myocardial infarction
	I22	Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
Pulmonary HTN	I27.0	Primary pulmonary hypertension
	I27.2	Other secondary pulmonary hypertension
Heart failure	I50	Heart failure
OSA	G47.33	Obstructive sleep apnea

References

1. Veasey, S.C. and I.M. Rosen, *Obstructive Sleep Apnea in Adults.* N Engl J Med, 2019. **380**(15): p. 1442-1449.
2. Marso, S.P., et al., *Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes.* N Engl J Med, 2016. **375**(19): p. 1834-1844.
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4. Gerstein, H.C., et al., *Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial.* Lancet, 2019. **394**(10193): p. 121-130.
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Results

Key Characteristics after Matching

	GLP-1 RA grp	Non-GLP-1 RA grp	SMD
Age at OSA diagnosis	54.8 ± 11.8	55.7 ± 13.0	0.07
Gender – Male	43.7%	42.2%	0.03
BMI (kg/m²)	40.7 ± 7.7	40.8 ± 7.7	0.01
HbA1c	7.6 ± 2.0	7.5 ± 2.0	0.08
Insulin/analogue use	44.0%	47.3%	0.06
Past Medical History			
Ischemic heart disease	13.7%	14.4%	0.02
Cerebrovascular disease	5.0%	5.2%	0.01
Hypertension	74.7%	78.1%	0.08

GLP-1RA used: liraglutide (50.2%)>dulaglutide (36.1%)>semaglutide (20.1%)

Key Primary and Secondary Outcomes

	GLP-1 RA (N= 16,881)	Non-GLP-1 RA (N= 16,881)	HR (95% CI)	P
Death from all cause	449	854	**0.505** (0.45-0.57)	<0.001
Newly diagnosed				
Acute MI	324	482	**0.645** (0.56-0.74)	<0.001
Heart Failure	1,206	1,579	**0.727** (0.67-0.78)	<0.001
Pulmonary HTN	329	499	**0.632** (0.55-0.73)	<0.001

Figure 1A. Survival curve for death from all cause

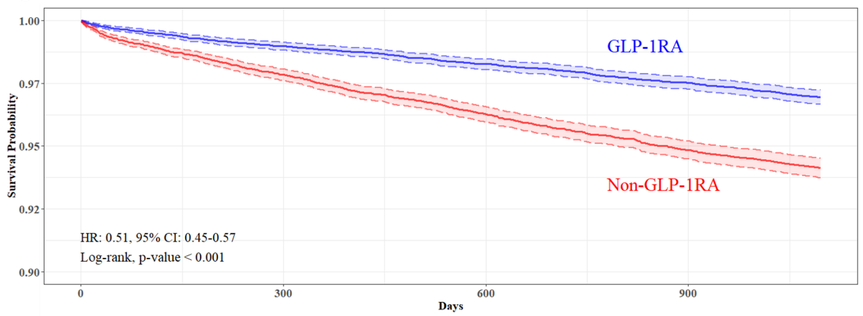


Figure 1B. Survival curve for acute myocardial infarction

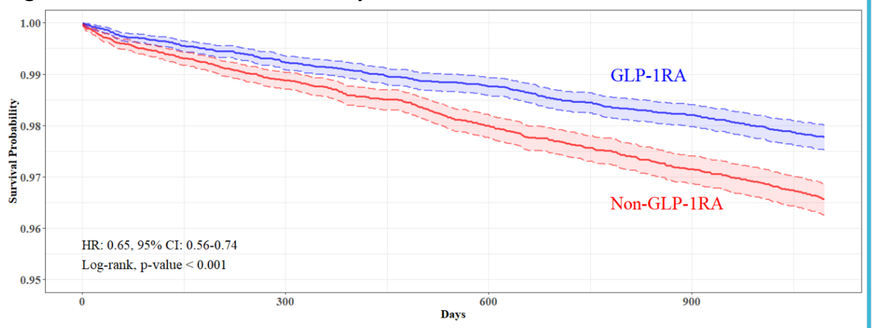


Figure 1C. Survival curve for heart failure

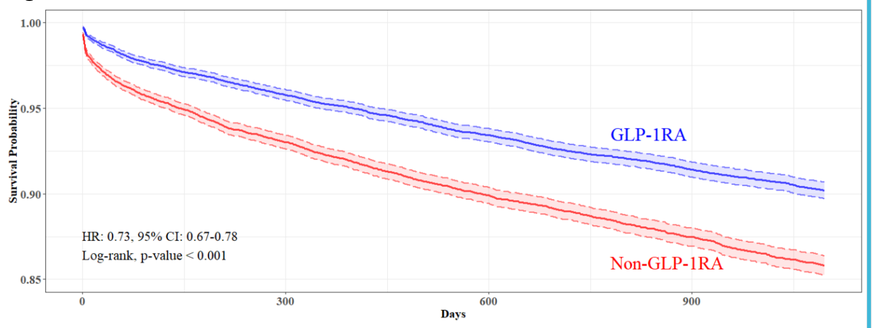
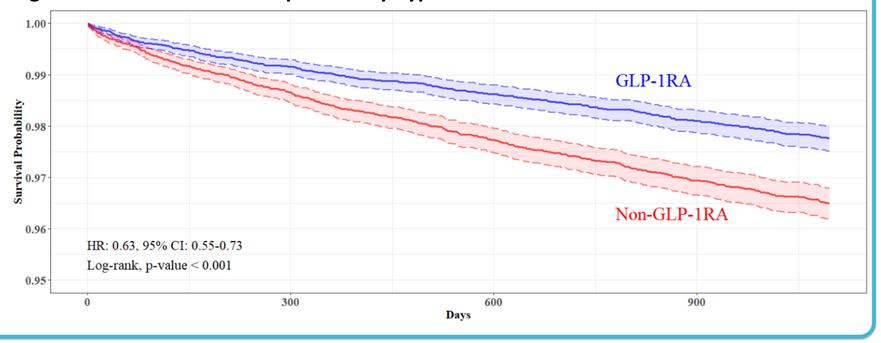


Figure 1D. Survival curve for pulmonary hypertension



Conclusions & Implication

- In obese patients with OSA, GLP-1RA use was associated **with lower risk of death from all cause and new onset acute myocardial infarction, heart failure, pulmonary hypertension (P<0.001).**
- Given early separation in survival, likely there is **direct mechanism of lowering cardiovascular risk** other than weight loss.
- Emerging data supporting **anti-inflammatory activity** of GLP-1 RAs, but given their mechanism of action, study comparing cardiovascular benefit of **starvation vs. GLP-1 RA use** might be helpful
- Real-patient data-based prospective study including pertinent data, such as procedural data reflecting surrogate marker for cardiovascular condition, PAP data, weight and A1c trending, is required for validation
- Still limitations exist: 1. Based on ICD-10 codes with underlying possibility of misclassification 2. Missing pertinent data including PAP usage data or chronological change of body weight or BMI 4. Limited generalizability as this study was performed on obese OSA patient only.

For any questions, please contact ahnj@odu.edu