

Real-world Evidence On GLP-1 Receptor Agonist Use And Mortality In Patients With Dementia

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INTRODUCTION

Metabolic dysfunction is increasingly recognized as a modifier of neurodegenerative disease progression. GLP-1 receptor agonists (GLP-1RAs), widely used in metabolic disorders, have been proposed as modulators of neuroinflammation, vascular risk, and systemic resilience through direct CNS receptor activity. However, real-world data examining their association with survival in patients with established dementia remain limited.

METHODS

Retrospective cohort study using the TriNetX Global Collaborative Network. Patients with dementia (Alzheimer's disease, vascular dementia, frontotemporal dementia, or dementia with Lewy bodies) were stratified by GLP-1RA exposure versus no exposure. The index event was the first recorded dementia diagnosis, with outcomes assessed after a 180-day wash-in period. Cohorts were balanced 1:1 by propensity score matching for demographics, neurological and systemic comorbidities, metabolic conditions including diabetes mellitus, and CNS medication use. Primary outcome was all-cause mortality.

RESULTS

After matching, 4,940 patients were included per cohort, with excellent balance at baseline including diabetes prevalence. All-cause mortality occurred in 18.2% of GLP-1RA-exposed patients versus 21.1% in non-exposed controls (risk difference -2.9%, 95% CI -4.6 to -1.3). Kaplan-Meier analysis demonstrated lower hazard of death in GLP-1RA users (HR 0.67, 95% CI 0.61-0.74; log-rank p < 0.001), with longer median survival in the exposed group (Figure 1).

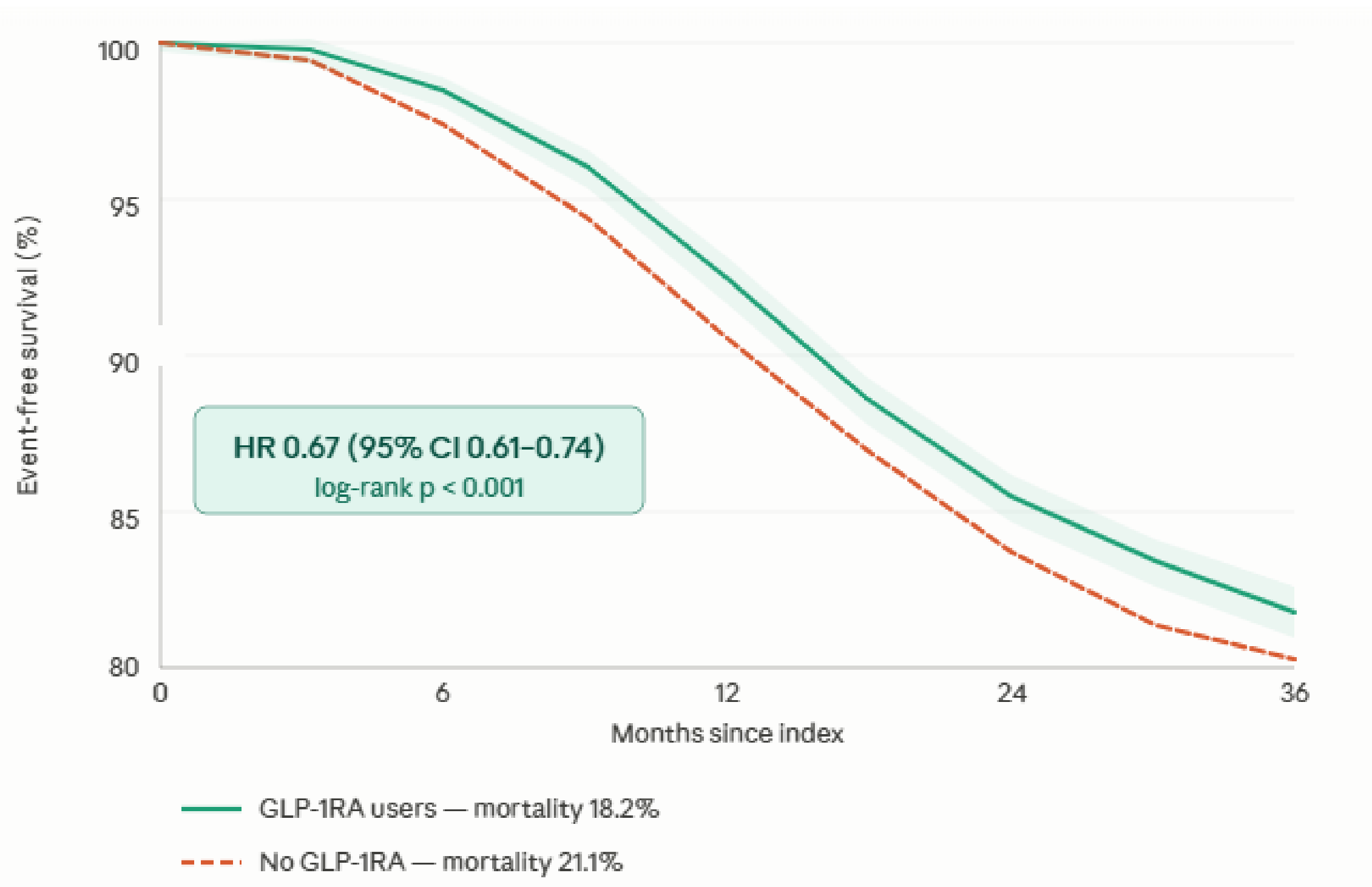


Figure 1. Illustrative Kaplan-Meier survival curves for all-cause mortality in propensity score-matched cohorts of GLP-1 receptor agonist users and non-users among patients with dementia. Curves are modeled from reported event rates; HR estimated by Cox regression.

CONCLUSIONS

GLP-1RA exposure in patients with dementia was associated with lower all-cause mortality in this large real-world cohort. These exploratory findings highlight a potential interaction between metabolic therapies and neurological outcomes. Future analyses will refine exposure definitions, stratify by dementia subtype, and explore metabolic and vascular effect modifiers.

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