Comparison of Change in Cardiac Injury Marker in Glucagon-Like Peptide-1 Receptor Agonist, Sodium-Glucose Cotransporter-2 Inhibitor, and Dipeptidyl Peptidase IV Inhibitor Users in a Real World Database

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BACKGROUND

Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RAs) are FDA approved for the treatment of Type 2 Diabetes Mellitus (T2DM) and obesity, and in 2024 Semaglutide has become the first GLP-1 RA indicated to treat cardiovascular disease (CVD). Sodium-Glucose Cotransporter-2 Inhibitor (SGLT2s) are indicated to treat T2DM and certain SGLT2s are now approved to treat CVD after showing significant improvements in clinical trials. Dipeptidyl Peptidase IV Inhibitors are diabetes drugs that have thus far shown no known effect on CVD outcomes. T2DM is associated with an elevated risk of cardiovascular events, which has been linked to increased levels of lactate dehydrogenase (LDH), an enzyme whose concentration rises in response to tissue damage and inflammation. The aim of this study was to compare how these three classes of drugs effect cardiovascular health as observed by changes in LDH after a one year period in a real world dataset from the University of California Health (UC Health) system.

OBJECTIVES

- Observe and compare change in LDH levels of GLP-1 RA, SGLT2, and DPP4 users from baseline to after a 1 year period.
- Observe how the proportion of individuals with elevated LDH levels changes across the three classes of drugs.

METHODS

1. **UC Health Data Warehouse** Utilized electronic health records of over 11 million California patients using Observational Health Data Informatics (OHDSI) codes and OMOP standardization.
2. **Inclusion Criteria**
   - Must have no overlapping use during the study period nor any previous use of any of the three classes of drugs.
   - Must have diabetes or obesity prior to or day of drug initiation.
   - All individuals are required to have at least 4 fills within the 1 year after first drug date.
   - Require at least one LDH within 4 weeks preceding first drug use and at least one LDH reading between 52-65 weeks after their first drug usage.
   - Comorbidities determined by ICD10 codes, measurements, or string search.
3. **Analysis** All analyses were conducted using SQL and R version 3.6.3 (R Project for Statistical Computing).

RESULTS

	GLP-1 RA	SGLT2i	DPP4i
N	69	52	61
Age	61.6	65.2	63.7
Female	42%	23%	39%
White	48%	65%	49%
Asian	7%	17%	13%
Black	9%	2%	8%
Other Race	30%	15%	21%
Unknown Race	6%	0%	8%
Diabetes	74%	73%	79%
Obesity	84%	71%	64%
Previous CVD	43%	75%	52%
Cancer	26%	35%	44%
Liver Disease	13%	8%	18%
Hyperlipidemia	64%	85%	66%
Hypertension	81%	88%	89%
Anticoagulants	80%	87%	72%
ACE Inhibitors	43%	46%	57%

Figure 1. Table 1 of Baseline Information

1. Figure 1
   - We can observe that SGLT2i users have fewer women compared to GLP-1 RA and DPP4i.
   - A larger percentage of SGLT2i users were White compared to GLP-1 RA and DPP4i users.
   - GLP-1 RA and DPP4i users had a lower percentage of previously experiencing a cardiovascular event in comparison to SGLT2i.
2. Figure 2
   - The distribution of LDH measurements at the end of study has notably shifted to the left compared to the baseline LDH measurements.
   - The Distributions of baseline vs. end of study measurements for GLP-1 RA and DPP4i stay relatively the same.
3. Figure 3
   - The average change in LDH for SGLT2i and GLP-1 RA was statistically significant after one year of drug use with at least 4 fills within the year.
   - SGLT2i users had a significant difference in change in LDH compared to DPP4i, GLP-1 RA did not.
4. Figure 4
   - There was a notable drop in the percent of SGLT2i users having an elevated LDH at the end of the study, signaling better overall cardiovascular health.
   - No notable change was observed among DPP4i users, which is consistent with research findings.
5. Overall Observations
   - SGLT2i use was observed to be associated with better cardiovascular outcomes within this study.
   - GLP-1 RA users show some improvements statistical improvements.

RESULTS

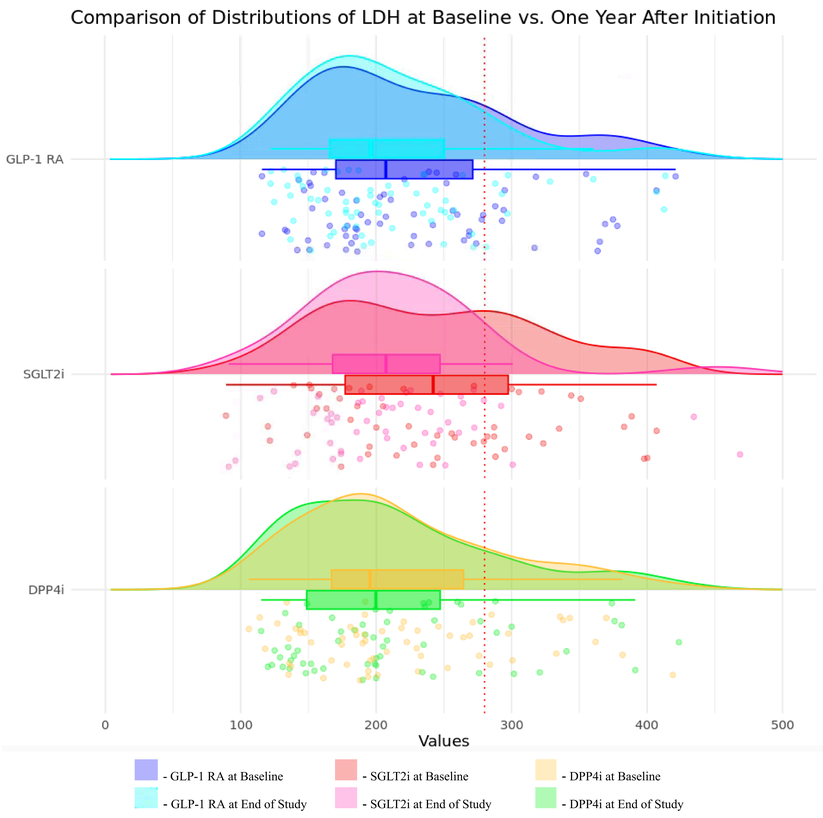

Figure 2. Comparing Baseline and End of Study Lactate Dehydrogenase Across the Classes of Drugs

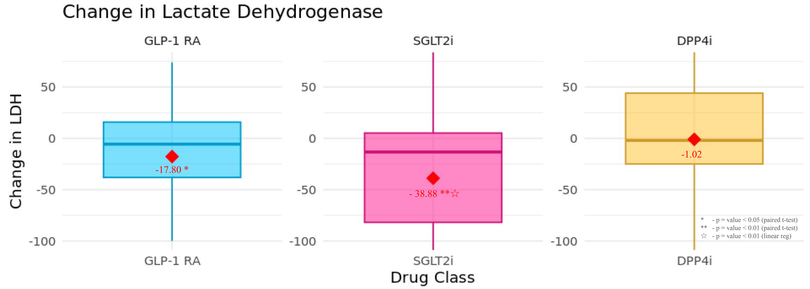

Figure 3. Difference in Lactate Dehydrogenase Levels at Baseline vs. Lactate Dehydrogenase Levels at End of Study

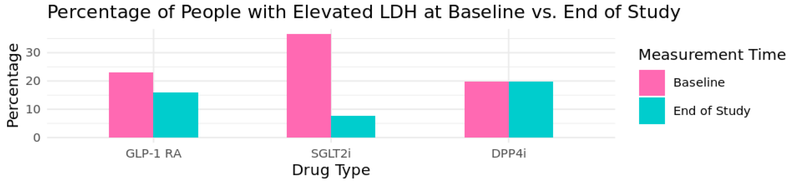

Figure 4. Percent of Users with Elevated LDH Before Index Date vs. After Index Date

CONCLUSION

Within this preliminary analysis, SGLT2is and GLP-1 RAs were observed to be linked to an overall average reduction in lactate dehydrogenase within diabetic and obese users. SGLT2is and GLP-1 RAs may play a valuable role in reducing the proportion of individuals with an elevated risk of cardiovascular disease.

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