**Abstract**

**Background**

Sodium-glucose cotransporter-2 inhibitors (SGLT2-Is) are medications commonly prescribed to treat type 2 diabetes mellitus (T2DM) given their proven cardiovascular and renal benefits. Clinical trials for empagliflozin have demonstrated reduced risk for decline in estimated glomerular filtration rate (eGFR), progression to macroalbuminuria, and incident albuminuria in veterans with cardiovascular disease. These trials did not report specific changes in urine albumin-to-creatinine (ACR) stratified by baseline levels or elucidate if there was an improvement in ACR after empagliflozin initiation. Thus, the purpose of this study was to evaluate the impact of empagliflozin on ACR and eGFR in a veteran population with varying degrees of albuminuria at the time of initiation.

**Methods**

This was a retrospective cohort study of veterans within the Durham VA Healthcare System with a diagnosis of T2DM who were initiated on empagliflozin between January 1, 2015 and August 31, 2020. Veterans were identified via SLQ query of the Corporate Data Warehouse based on ICD-9 and ICD-10 codes. Additional chart review was used for application of inclusion and exclusion criteria along with data collection. Last observation carried forward imputation used for missing data points. Baseline data points were compared to data at 6-, 12-, 24-, and 48-months post empagliflozin initiation.

**Objectives**

The primary objective of this study was to assess the change in urine ACR in veterans with T2DM on empagliflozin. Secondary objectives were to assess the change in ACR and eGFR in veterans with T2DM on empagliflozin at specified timepoints.

**Results**

482 veterans were identified as meeting inclusion criteria. The primary endpoint, change in ACR from baseline to 12 months in veterans with baseline ACR ≥30 mg/g, was -38.9 mg/g (p-value = 0.3). The decline in ACR in this group at 6 months was -55.0 mg/g (p-value = 0.0007). There was also a decline in ACR in veterans with a baseline ACR ≥300 mg/g at 6, 24, and 48 months (-206.3 mg/g, p-value 0.0003; -238.3 mg/g, p-value = 0.03; -232.6 mg/g, p-value = 0.04). In veterans with baseline ACR 30-300, ACR was higher at 24 and 48 months post-empagliflozin initiation (44.9 mg/g, p-value = 0.01; 44.9 mg/g, p-value = 0.01). Decline in eGFR was statistically significant at all timepoints regardless of baseline ACR. The results of other endpoints were not statistically significant.

**Discussion**

Impact of empagliflozin on ACR was variable based on timepoint and baseline ACR with the largest improvement in ACR seen in veterans with macroalbuminuria at the time of empagliflozin initiation. eGFR declined across all timepoints although the mean difference in eGFR from baseline to 48 months was similar to the decline seen in empagliflozin groups in EMPA-REG OUTCOME trial. The use of imputation for missing laboratory values may have impacted the results in the setting of extended monitoring intervals during the COVID-19 pandemic. Imputation was necessary for ≥42% of ACR data points which may explain why many results were not statistically significant and why ACR was higher in veterans with a baseline ACR of 30-300 mg/g at 24 and 48 months. The lack of data points indicates an opportunity for provider education given ADA guidelines recommend ACR monitoring in veterans with T2DM at least once yearly.