

# Patients with diabetes on SGLT2 inhibitors undergoing total knee replacement are at increased odds for a number of postoperative adverse events, but reduced risk of transfusion

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## INTRODUCTION:

Diabetes mellitus (DM) is a common comorbidity in patients undergoing total knee arthroplasty (TKA). In recent years, several new classes of medications have been approved to better manage DM. One such class of medications are SGLT2 inhibitors (SGLT2i), which inhibit reabsorption of glucose in the kidney. Examples of medications in this class include Jardiance, Invokana, and others. The present study aims to investigate the correlation of SGLT2i use on postoperative complications and revision rates in diabetic patients.

## METHODS:

Adult patients with a diagnosis of DM undergoing primary TKA for osteoarthritis were identified from the large, multi-insurance, administrative PearlDiver M157 database. Exclusion criteria included: age < 18 years, activity in the database < 90 days postoperative, and infections, neoplastic, or traumatic diagnoses within 90 days preoperative.

From this study population, two sub-cohorts were created: 1) patients with DM and a history of SGLT2i (canagliflozin, dapagliflozin propanediol, empagliflozin, or ertugliflozin pidolate) use, 2) patients with DM but no history of SGLT2i use. The two sub-cohorts were matched 1:4 based on age, sex, and Elixhauser Comorbidity Index (ECI). Differences in 90-day postoperative adverse outcomes (specifically myocardial infarction [MI], sepsis, cardiac arrest, pulmonary embolism [PE], deep vein thrombosis [DVT], surgical site infection [SSI], urinary tract infection [UTI], pneumonia, acute kidney injury [AKI], hematoma, wound dehiscence, and transfusion) were assessed with multivariable logistic regression controlling for patient age, sex, ECI, tobacco use, long-term insulin use, obesity, and metformin use. Five-year implant survival was assessed utilizing Kaplan-Meier analysis.

## RESULTS SECTION:

A total of 164,474 TKA patients with DM were identified, of which 9,246 (5.6%) were taking SGLT2i. After matching, in the final study cohort the number of patients without SGLT2i use was 36,804 (80%), while the number of patients with SGLT2i use was 9,207 (20%).

On multivariable analysis, DM patients using SGLT2i had higher odds of aggregated adverse events driven by MI (OR 2.37,  $p < 0.0001$ ), sepsis (OR 1.68,  $p < 0.0001$ ), UTI (OR 2.00,  $p < 0.0001$ ), pneumonia (OR 1.80,  $p < 0.0001$ ), AKI (OR 1.27,  $p < 0.0001$ ), but had lower odds of transfusion (OR 0.28,  $p < 0.0001$ ) (Figure). Five-year survival to revision TKA were not significantly different between the matched cohorts.

## DISCUSSION:

TKA patients with DM who were taking SGLT2i were associated with increased risk of several adverse events, including MI, sepsis, UTI, pneumonia, and AKI, but decreased odds of transfusion. Some of these adverse events are consistent with established side effects of the medication, such as UTI. However, some results conflict with previous studies showing SGLT2i to be protective against cardiovascular adverse events. The reduced odds of transfusion are consistent with previously published reports of SGLT2i increasing hemoglobin levels in patients with type 2 DM and chronic kidney disease.

Despite the limitations of the present study (retrospective study based on administrative data), these results provide data on previously unreported potential increased risks that can be used to guide surgical decision-making and patient counseling for patients taking SGLT2i, while also demonstrating the need for further investigation of these medications in a surgical setting.

## SIGNIFICANCE/CLINICAL RELEVANCE:

As new medications are introduced to treat common chronic comorbidities such as DM, it is important to investigate the potential benefits and risks to surgical candidates. The present study is the first to use a large database to investigate the odds of postoperative adverse events in TKA patients taking SGLT2i, providing additional information to be used by providers and patients in surgical decision making.

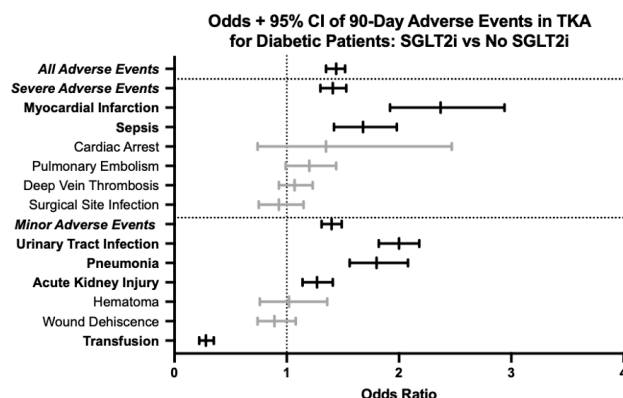


Figure: Forest plot of OR and 95% for multivariable analysis of 90-day adverse events following TKA for diabetic patients with and without SGLT2 inhibitor use