Unlocking the Survival Advantage: Angiotensin Receptor Blockers Reduce Mortality Threefold After Knee Arthroplasty

Alireza Mirahmadi, Jad Jack Lawand, Kaveh Momenzadeh, Mohamad Javad Shariati, Ara Nazarian

INTRODUCTION: Total knee arthroplasty (TKA) is a widely performed procedure with excellent functional outcomes, yet systemic complications remain a concern—particularly in patients with cardiovascular comorbidities. The renin-angiotensin-aldosterone system (RAAS) plays a central role in inflammatory signaling, vascular homeostasis, and organ-specific responses to surgical stress. Angiotensin-converting enzyme inhibitors (ACEis) and angiotensin II receptor blockers (ARBs) are among the most prescribed antihypertensive medications, but their class-specific impact on postoperative medical complications remains unclear. This study aimed to evaluate the effects of perioperative ACEi or ARB use on systemic outcomes after TKA, including short-term and long-term complications across cardiovascular, renal, and hepatic domains, as well as overall mortality.

METHODS:

We performed a retrospective cohort study using the TriNetX Research Network, a federated database of deidentified electronic health records from healthcare institutions across the United States. Adult patients undergoing primary TKA between 2005 and 2025 were identified using standardized ICD-10 and CPT codes. Perioperative ACEi or ARB use was defined as an active prescription within 3 months before or after surgery. Four matched comparisons were constructed: (1) ACEi/ARB vs. no ACEi/ARB, (2) ACEi vs. no ACEi, (3) ARB vs. no ARB, and (4) ACEi vs. ARB. Propensity score matching (1:1) was performed based on age, sex, race, BMI, comorbidities (e.g., diabetes, hypertension), and concurrent medications.

Short-term outcomes assessed at 90 days included emergency department (ED) visits, readmissions, and mortality. Long-term outcomes assessed at 2 years included myocardial infarction (MI), stroke, acute renal failure, liver failure, and all-cause mortality. Statistical comparisons were conducted using chi-square and t-tests, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Statistical significance was defined as $P < 0.01$.

RESULTS:

Following matching, the study included 105,072 patients for 90-day follow-up and 75,277 patients for 2-year follow-up. Cohorts were well balanced in demographics (mean age 66.6–67.0 years, 59% female, BMI ~33; $P > 0.05$). In the combined ACEi/ARB cohort, 90-day outcomes revealed lower rates of ED visits (7.7% vs. 8.1%; OR 0.96; $P = 0.007$), readmissions (1.6% vs. 1.8%; OR 0.90; $P = 0.001$), and mortality (0.2% vs. 0.6%; OR 0.34; $P < 0.001$) compared to controls.

At 2-year follow-up, the ACEi/ARB group showed a significantly lower mortality rate (0.5% vs. 1.5%; OR 0.35; $P < 0.001$) despite higher incidences of myocardial infarction (1.6% vs. 0.9%; OR 1.68; $P < 0.001$), stroke (1.7% vs. 1.5%; OR 1.16; $P < 0.001$), and acute renal failure (5.0% vs. 3.0%; OR 1.62; $P < 0.001$).

Subgroup analyses indicated that ARBs were responsible for the majority of protective effects, including lower mortality and fewer short-term readmissions and ED visits. Conversely, adverse events such as MI, stroke, and renal failure were primarily associated with ACEi use. Direct comparison confirmed that ARBs outperformed ACEis in reducing systemic complications and mortality.

Despite increased rates of certain medical complications, patients on RAAS inhibitors—particularly ARBs—exhibited a strikingly lower risk of mortality in both short- and long-term periods. This finding underscores a potentially meaningful systemic protective effect, warranting further mechanistic and prospective investigation.

DISCUSSION AND CONCLUSION:

Perioperative use of ACE inhibitors and ARBs was associated with divergent effects on systemic outcomes following TKA. While patients on RAAS inhibitors experienced higher incidences of cardiovascular and renal complications—particularly those on ACEis—both drug classes were linked to a significantly lower risk of mortality. Notably, ARBs consistently outperformed ACEis in minimizing adverse events, including ED visits, readmissions, and mortality, highlighting a possible class-specific protective effect.

These findings have important clinical implications. For patients with cardiovascular risk factors undergoing TKA, ARBs may offer a dual benefit: effective blood pressure control and reduced risk of postoperative mortality. The potential trade-off between increased non-lethal complications and improved survival suggests that careful perioperative medication management may enhance outcomes.

Future prospective studies should investigate the mechanistic basis of ARBs' protective effects, explore optimal timing and duration of perioperative RAAS inhibition, and evaluate whether strategic switching from ACEis to ARBs can mitigate surgical risk in orthopedic populations.