Second Generation Antidepressants Significantly Increase the Risk of Postoperative Complications in Total Knee Arthroplasty

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INTRODUCTION:
Selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) are the most commonly prescribed antidepressants in the United States currently. With recent evidence indicating that SSRIs and SNRIs significantly impact bone health and quality, we sought to evaluate their effect on 90-day postoperative outcomes following total knee arthroplasty.

METHODS:
The TrinetX research network was queried to identify patients who underwent primary total knee arthroplasty (TKA) between January 2004 - May 2024 across 89 organizations. Three comparison groups were established based on antidepressant prescription within a year of index TKA – patients on SSRIs exclusively, SNRIs exclusively, and no prescription of SSRIs or SNRIs (control). Intergroup comparisons were made after performing a comprehensive 1:1 propensity score matching to account for differences in demographics and medical comorbidities for each sub-analysis.

RESULTS: The SSRI–control and SNRI–control matched cohorts comprised 33,743 and 16,591 patients, respectively. The SSRI vs. SNRI cohort consisted of 16,063 matched pairs. On performing multivariable logistic regression analysis, SSRI patients were found to have higher risks of ED utilization (7.8 vs. 6.5%, p<0.001), revision (0.7 vs. 0.5%, p<0.001), joint infection (1.1 vs. 0.8%, p<0.001), acute renal failure (1.7 vs. 1.4%, p=0.003), and aspiration (0.2 vs. 0.1%, p=0.013) within 90 days of TKA. SNRI patients had similarly higher risks of ED utilization (8.1 vs. 6.7%, p=0.001), revision (0.8 vs. 0.5%, p<0.001), joint infection (1.3 vs. 0.8%, p<0.001), acute renal failure (1.7 vs. 1.4%, p=0.048), and aspiration (0.2 vs. 0.1%, p=0.019) (**Table 1**). Readmission, mortality, superficial surgical site infection, deep venous thrombosis, and pulmonary embolism risks were similar between patients with and without antidepressant use, irrespective of the drug. SNRI patients had a higher risk of postoperative joint infection than SSRI patients (1.3 vs. 1.1%, p=0.047) (**Table 2**).

DISCUSSION AND CONCLUSION: This study demonstrated significantly worse outcomes among TKA patients with preoperative SSRI and SNRI prescriptions. Our findings may assist in refining preoperative optimization practices, consequently improving outcomes following TKA.

Table 1. Risk of 90-day complications in total knee arthroplasty patients with preoperative selective serotonin reuptake inhibitor or serotonin and norepinephrine reuptake inhibitor use

Outcome	Antidepressant use (%)	No antidepressant (%)	P-value
SSRI use			
Readmission	1.7	1.5	.191
ED utilization	7.8	6.5	**<.001**
Revision	0.7	0.5	**<.001**
Mortality	0.3	0.3	.197
Preprosthetic joint infection	1.1	0.8	**<.001**
Superficial surgical site infection	0.3	0.2	.142
Deep venous thrombosis	0.9	0.9	.704
Pulmonary Embolism	0.6	0.5	.351
Acute renal failure	1.7	1.4	**0.003**
Aspiration	0.2	0.1	**0.013**
SNRI use			
Readmission	1.7	1.5	.056
ED utilization	8.1	6.7	**.001**
Revision	0.8	0.5	**<.001**
Mortality	0.3	0.2	.123
Preprosthetic joint infection	1.3	0.8	**<.001**
Superficial surgical site infection	0.3	0.3	.521
Deep venous thrombosis	0.9	1.0	.370
Pulmonary Embolism	0.5	0.5	.404
Acute renal failure	1.7	1.4	**0.048**
Aspiration	0.2	0	**0.019**

Table 2. Comparison between risk of 90-day complications in total knee arthroplasty patients using selective serotonin reuptake inhibitors and serotonin and norepinephrine reuptake inhibitors.

Outcome	SSRI use (%)	SNRI use (%)	P-value
Readmission	1.7	1.7	.891
ED utilization	7.8	8.0	.651
Revision	0.7	0.8	.317
Mortality	0.3	0.3	.421
Preprosthetic joint infection	1.1	1.3	**.047**
Superficial surgical site infection	0.2	0.3	.321
Deep venous thrombosis	1.0	0.9	.475
Pulmonary Embolism	0.6	0.5	.328
Acute renal failure	1.6	1.7	.536
Aspiration	0.2	0.2	.997