Preoperative Benzodiazepine Use Increases Risk of Complications Following Primary Total Hip Arthroplasty

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INTRODUCTION: Benzodiazepines suppress osteogenesis and may contribute to complications after orthopedic procedures, though this relationship remains poorly defined. This study aimed to characterize the relationship between benzodiazepine use and surgical complications following total hip arthroplasty (THA).

METHODS: Using the PearlDiver administrative claims database (2010 to 2023), we identified 51,145 primary THA patients without osteoporosis who filled a benzodiazepine prescription within 60 days before surgery. Patients were matched 1:4 with Benzodiazepine-naive patients by age, sex, Charlson Comorbidity Index, cognitive disorders, depression, anxiety, and substance abuse. Daily doses were standardized by quantity, days supplied, and strength, then categorized as low (0-2mg), medium (2-4mg), or high (>4mg). Multivariate regression and Kaplan–Meier analyses evaluated surgical complications and revision-free survival at 2 years.

RESULTS: We included 44,247 benzodiazepine users (65.3 ± 10.1 years) with 2-year follow-up, matched to 174,264 controls. Anxiety (60.5% vs 59.8%, *P*=0.105) and depression (50.7% vs 50.4%, *P*=0.408) were comparable amongst cohorts. Benzodiazepine users exhibited significantly higher rates of PJI (1.1% vs 1.0%, *P*=0.006), dislocation (1.4% vs 1.0%, *P*<0.001), fracture (0.64% vs 0.57%, *P*<0.001) and revision (1.5% vs 1.3%, P<0.001) at 2 years. Benzodiazepine use independently increased odds of any complication at 2 years (OR=1.29; *P*<0.001). Dose-dependent relationships emerged for aggregate complications and were strongest for dislocation (2-year high-dose: OR=1.62; *P*<0.001). No dose effect was seen for loosening, PJI, or fracture (all *P*>0.224). Benzodiazepine use significantly decreased revision-free implant survival at 2 years (*P*<0.001).

DISCUSSION AND CONCLUSION: Preoperative benzodiazepine use is independently associated with increased risk of surgical complications at short term follow up, particularly dislocation, with a dose-dependent relationship. Orthopaedic surgeons should recognize and counsel patients on the increased risk of complications associated with benzodiazepines.

Table 1. Patient Demographics

n, % unless otherwise specified	Preop Benzo Use (*n* = 44,247)	Controls (*n* = 174,264)	*P*-value
Age (mean, SD)	65.3 ± 10.1	65.4 ± 10.0	0.241
CCI (mean, SD)	1.5 ± 1.9	1.5 ± 1.8	<0.001
Male gender	17,378 (39.3%)	68,261 (39.2%)	0.693
Cognitive Disorder‡	6,235 (14.1%)	23,972 (13.8%)	0.069
Substance Abuse	12,198 (27.6%)	47,328 (27.2%)	0.085
Anxiety	26,662 (60.3%)	104,268 (59.8%)	0.105
Depression	22,409 (50.7%)	87,870 (50.4%)	0.408

Abbreviations: CCI, Charlson Comorbidity Index; SD, standard deviation.
‡ Includes dementia, Alzheimer's, and other degenerative brain disorders

Table 2. Two-Year Outcomes

n, % unless otherwise specified	Preop Benzo Use (*n* = 44,247)	Controls (*n* = 174,264)	*P*-value
Any 2-Year Complication	2,131 (4.82%)	6,941 (3.98%)	**<0.001**
Loosening	206 (0.47%)	749 (0.43%)	0.328
Periprosthetic Fracture	285 (0.64%)	992 (0.57%)	**<0.001**
PJI	627 (1.42%)	2,153 (1.24%)	**0.003**
Dislocation	857 (1.94%)	2,280 (1.31%)	**<0.001**
Revision THA	1,044 (2.36%)	3,286 (1.89%)	**<0.001**

Abbreviations: PJI, periprosthetic joint infection; THA, total hip arthroplasty.

Table 3. Multivariate-adjusted primary outcomes by Benzodiazepine daily dose

	2 Year Outcomes		
Odds ratio (95% CI; P-value)	**Low (*n* = 53,530)**	**Medium (*n* = 7,602)**	**High (*n* = 14,623)**
Any 2 Year Complication	**1.20 (1.03-1.41; *P* = 0.021)**	**1.15 (1.01-1.31; *P* = 0.033)**	**1.29 (1.15-1.43; *P* < 0.001)**
Loosening	1.00 (0.58-1.61; *P* = 0.999)	0.97 (0.64-1.43; *P* = 0.870)	1.03 (0.73-1.44; *P* = 0.868)
Periprosthetic Fracture	0.89 (0.55-1.38; *P* = 0.632)	1.10 (0.78-1.53; *P* = 0.571)	1.13 (0.84-1.50; *P* = 0.409)
PJI	1.26 (0.94-1.67; *P* = 0.107)	**1.41 (1.13-1.75; *P* = 0.002)**	1.20 (0.98-1.47; *P* = 0.072)
Dislocation	**1.36 (1.05-1.73; *P* = 0.015)**	**1.36 (1.11-1.65; *P* = 0.002)**	**1.62 (1.37-1.91; *P* < 0.001)**

Adjusted for age, sex, Charlson Comorbidity Index score, obesity, and presence of cognitive disorders, anxiety disorders, depression, and substance abuse. Daily dose categories were compared to a reference group with a daily dose of 0. Doses were calculated as: (quantity / days supply) × strength prescribed. Dose categories: low = 0–2mg, medium = 2–4mg, high > 4mg.
Abbreviations: PJI, periprosthetic joint infection; THA, total hip arthroplasty; CI, confidence interval.

Figure 1. Kaplan-Meier analysis for revision free survival at 2 years for 2-year cohort