Which Oral Drugs Associated with Adverse Effects on Bone Mineral Density Demonstrate Worse Total Knee Arthroplasty Implant-Related Complications?

Emile Kuyl, Philip M Parel, Amil Raj Agarwal, Alex Gu[1], Andrew Harris, Sandesh Rao, Gregory Golladay[2], Savyasachi C Thakkar

[1]George Washington University School of Medicine An, [2]VCU Health

INTRODUCTION: Certain medications interfere with the bone remodeling process, and thus increase the risk of bone-health related complications. As patients undergoing total knee arthroplasty (TKA) may be taking these bone mineral density (BMD) reducing medications, it is unclear as to whether and which medications impact TKA outcomes. Therefore, the purpose of this study was to observe the impact of various BMD reducing medications on 2-year implant-related complications following TKA.

METHODS: A retrospective analysis of patients undergoing primary elective TKA was conducted using a national administrative claims database. Patients were identified if they were taking any of these known BMD reducing medications in the perioperative period: proton pump inhibitors (PPIs), thiazolidinediones (TZDs), loop diuretics, systemic corticosteroids, aromatase inhibitors (AIs), calcineurin inhibitors, selective serotonin reuptake inhibitors (SSRIs), antiepileptic drugs (AEDs), first-generation antipsychotics (FGAs), and second-generation antipsychotics (SGAs). The 2-year incidence of all-cause revision and aseptic indications for revision (aseptic loosening and periprosthetic fracture [PPF]) were compared using chi-squared analysis for each drug class when compared to a control of those not taking any of these identified medications. To control for demographics/comorbidities and confounders associated with taking multiple agents (Table 1), multivariable logistic regression analyses were conducted for each 2-year outcome with the output recorded as odds ratios (OR).

RESULTS: Of the 1,118,832 TKA patients identified, 478,180 (42.7%) were taking at least one BMD reducing medication. Patients taking BMD reducing drugs were younger (65.7 versus 66.4 years; p-value <0.001), less likely to be male (31.33% versus 41.50%; p-value <0.001), and to have greater comorbidities (all with a p-value <0.001). On multivariable analysis, medications associated with a higher likelihood of 2-year all-cause revision include PPIs (OR: 1.5), systemic corticosteroids (1.15), SSRIs (OR: 1.14), FGAs (OR: 1.54), and SGAs (OR: 1.29) (p<0.05 for all). Medications associated with a higher likelihood of 2-year aseptic loosening indication revision include PPIs (OR: 1.16), systemic corticosteroids (OR: 1.17), SSRIs (OR: 1.09), and SGAs (OR: 1.12) (p<0.05 for all). Medications associated with a higher likelihood of 2-year PPF indicated revision include PPIs (OR: 1.81), AIs (OR: 1.40), SSRIs (OR: 1.25), FGAs (OR: 1.48), and SGAs (1.47) (p<0.05 for all).

DISCUSSION AND CONCLUSION: Of the drug classes observed, the utilization of perioperative PPIs, SSRIs, systemic corticosteroids, FGAs, and SGAs were associated with the highest odds of all-cause revision and aseptic loosening-indicated revision, and PPF-indicated revision. As almost half of patients are taking at least one of these medications, our findings emphasize the importance of reviewing patients medication usage and highlights specific medications to look out for during review.

Figure 1: Multivariate logistic regression analysis of 2-year all-cause revision for patients taking BMD reducing medications versus controls (*PPIs = proton pump inhibitors, TZD = thiazolidinediones, AIs = aromatase inhibitors, AEDs = antiepileptic inhibitors, SSRIs = selective serotonin reuptake inhibitors, FGAs = first-generation antipsychotics, SGAs = second-generation antipsychotics*)

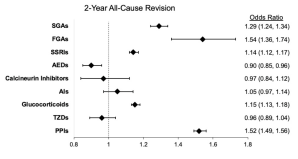

Figure 2: Multivariate logistic regression analysis of 2-year PPF-indicated revision for patients taking BMD reducing medications versus controls (*PPIs = proton pump inhibitors, TZD = thiazolidinediones, AIs = aromatase inhibitors, AEDs = antiepileptic inhibitors, SSRIs = selective serotonin reuptake inhibitors, FGAs = first-generation antipsychotics, SGAs = second-generation antipsychotics*)

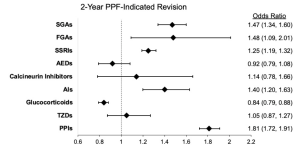

Figure 3: Multivariate logistic regression analysis of 2-year loosening-indicated revision for patients taking BMD reducing medications versus controls (*PPIs = proton pump inhibitors, TZD = thiazolidinediones, AIs = aromatase inhibitors (AIs), AEDs = antiepileptic inhibitors, SSRIs = selective serotonin reuptake inhibitors, FGAs = first-generation antipsychotics, SGAs = second-generation antipsychotics*)

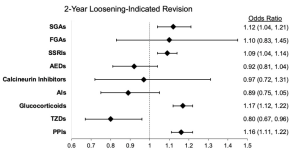

Table 1: Demographic and comorbidity characteristics of primary TKA patients taking at least 1 BMD reducing medication versus controls

	BMD Reducing Drugs		Control		
	N	%	N	%	p-value
Total	478,180	-	710,652	-	-
Demographic and Comorbidity Characteristics					
Age (Mean±SD)	65.7 ± 9.0	-	66.4 ± 8.7	-	**<0.001**
Sex	-	-	-	-	-
Men	149,828	31.33	294,955	41.50	-
Women	328,352	68.67	415,697	58.50	**<0.001**
Diabetes Mellitus	39,155	8.19	48,013	6.76	**<0.001**
Tobacco Use	16,357	3.42	17,256	2.43	**<0.001**
Chronic Kidney Disease	19,633	4.11	21,309	3.00	**<0.001**
Obesity	42,820	8.95	50,163	7.06	**<0.001**
Depression	36,986	9.90	36,986	5.20	**<0.001**
Anemia	19,233	4.02	20,929	2.95	**<0.001**
Congestive Heart Failure	18,506	3.87	16,703	2.35	**<0.001**
Hypertension	75,721	15.84	101,523	14.29	**<0.001**
Arrhythmia	40,173	8.40	50,457	7.10	**<0.001**
Neurological Disorder	8,847	1.85	8,561	1.20	**<0.001**
Psychosis	4,503	0.94	3,336	0.47	**<0.001**
Peptic Ulcer Disease	2,485	0.52	2,595	0.37	**<0.001**
Rheumatoid Arthritis	21,747	4.55	21,035	2.96	**<0.001**