Impact of Osteoporosis Medications on Postoperative Complications Following TKA

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INTRODUCTION: Bisphosphonates have been the gold standard for osteoporosis treatment in the past decade. However, other medications available on the market have also shown to be valuable in the treatment of osteoporosis through different mechanisms. Knowledge is limited in regards to the incidence of postoperative complications following total knee arthroplasty (TKA) for patients taking these osteoporosis medications regularly. As such, we examined: (1) What is the incidence of post-TKA complications in patients taking Denosumab, SERMs, or Teriparatide, and Bisphosphonates at 90 days, 1 year, and 2 years? (2) What are the odds of post-TKA complications in patients taking Denosumab, SERMs, or Teriparatide, at 90 days, 1 year, and 2 years compared to Bisphosphonates?

METHODS: Employing a retrospective cohort design, we used an all-payer national database to identify 28,514 post-TKA osteoporotic patients from 2015-2022 who were taking either bisphosphonates, denosumab, SERMs, or teriparatide. Inclusion criteria included TKA and a diagnosis of osteoporosis. prescription of bisphosphonates, denosumab, SERMS, or teriparatide. Exclusion criteria included a history of knee fracture, TKA due to trauma, or age under 18. Postoperative complications investigated for each osteoporosis medication included prosthetic joint infection (PJI), surgical site infection (SSI), aseptic revision, manipulation under anesthesia (MUA), aseptic loosening, venous thromboembolism (VTE), and periprosthetic fracture (PPFx).

RESULTS:

There was a higher incidence of PJI in post-TKA patients taking teriparatide (0.5% vs. 0.1%, 0%, 0.1%, P=0.049) compared to TKA patients taking bisphosphonates, denosumab, or SERM's at 90 days, respectively. There was a higher incidence of aseptic revision in post-TKA patients taking denosumab (1.2% vs. 0.6%, 0.7%, 0.9%, P=0.033) compared to TKA patients taking bisphosphonates, SERM's or teriparatide at 90 days, respectively. There was a higher incidence of aseptic loosening in post-TKA patients taking teriparatide (0.3% vs. 0.01%, 0.1%, 0.1%, P=0.030) compared to TKA patients taking bisphosphonates, denosumab, or SERM's at 1 year, respectively. Additionally, when compared to bisphosphonates, denosumab showed higher odds of aseptic revision (OR=2.11, OR=1.54) at 90 days and 1 year, respectively. Teriparatide showed higher odds of PJI (OR=3.73, OR=2.52) at 90 days and 2 years, respectively, and aseptic loosening (OR=7.23) at 1 year.

DISCUSSION AND CONCLUSION:

Both teriparatide and denosumab showed a higher incidence and odds of certain post-TKA complications compared to bisphosphonates. The implications of our study are relevant when determining the best osteoporosis medication for a patient considering undergoing a TKA in their future. Addressing the shortcomings of the postoperative medication dependent complications can also improve the current state of practice by better selecting patients for TKA in a shared decision making conversation between the orthopaedic surgeon and patient.

Table 1. Demographics and Baseline Characteristics

	Control Bisphophonates (n=23,189)	Denosumab (n=1,209)	SERMs (n=3531)	Teriparatide (n=585)	*p-value*
	n (%)	*n (%)*	*n (%)*	*n (%)*	
Age (SD)	72(6.7)	70(6.6)	69(7.7)	71(6.3)	
Sex					<0.001
Female	21817 (94.1)	1161 (96.0)	3519 (99.7)	535 (91.5)	
Male	1372 (5.9)	48 (4.0)	12 (0.3)	50 (8.5)	
AA	864 (3.7)	44 (3.6)	97 (2.7)	39 (6.7)	<0.001
Cancer	5760 (24.8)	305 (25.2)	1442 (40.8)	113 (19.3)	<0.001
CKD	6665 (28.7)	348 (28.8)	908 (25.7)	164 (28.0)	0.003
COPD	9880 (42.6)	531 (43.9)	1392 (39.4)	272 (46.5)	<0.001
CHF	3098 (13.4)	126 (10.4)	398 (11.3)	92 (15.7)	<0.001
Diabetes	11091 (47.8)	576 (47.6)	1555 (44.0)	265 (45.3)	<0.001
Comp DM	5338 (23.0)	288 (23.8)	697 (19.7)	118 (20.2)	<0.001
Uncomp DM	8552 (36.9)	444 (36.7)	1181 (33.4)	199 (34.0)	0.001
HTN	20959 (90.4)	1063 (87.9)	3135 (88.8)	523 (89.4)	0.001
Hypothyroid	10264 (44.3)	616 (51.0)	1663 (47.1)	272 (46.5)	<0.001
RA	3501 (15.1)	239 (19.8)	368 (10.4)	120 (20.5)	<0.001
Obesity	10522 (45.4)	529 (43.8)	1517 (43.0)	226 (38.6)	0.001
TU	7901 (34.1)	376 (31.1)	1132 (32.1)	225 (38.5)	0.002
CAD	9165 (39.5)	500 (41.4)	1228 (34.8)	233 (39.8)	<0.001
Liver Disease	4451 (19.2)	272 (22.5)	680 (19.3)	121 (20.7)	0.033
Renal Disease	6862 (29.6)	355 (29.4)	939 (26.6)	171 (29.2)	0.004
Depression	10974 (47.3)	578 (47.8)	1617 (45.8)	322 (55.0)	0.001
Renal Failure	6851 (29.5)	355 (29.4)	939 (26.6)	171 (29.2)	0.005

AA: Alcohol Abuse; CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmonary Disease; CHF: Congestive Heart Failure; DM: Diabetes Mellitus; Comp: Complicated; Uncomp: Uncomplicated; HTN: Hypertension; RA: Rheumatoid Arthritis; TU: Tobacco Use; CAD: Coronary Artery Disease

Table 2. Incidences of Complications

	Control Bisphosphonates (n=23,189)	Denosumab (n=1,209)	SERMs (n=3531)	Teriparatide (n=585)	*p-value*
	n (%)	*n (%)*	*n (%)*	*n (%)*	
90 Complications					
PJI	32 (0.1)	0 (0)	4 (0.1)	3 (0.5)	0.049
SSI	110 (0.5)	6 (0.5)	14 (0.4)	6 (1.0)	0.240
Aseptic Revision	127 (0.6)	14 (1.2)	25 (0.7)	5 (0.9)	0.033
MUA	562 (2.4)	24 (2.0)	69 (2.0)	9 (1.15)	0.168
Aseptic Loosening	6 (0.03)	0 (0.0)	0 (0.0)	1 (0.2)	0.098
VTE	338 (1.5)	14 (1.2)	58 (1.6)	7 (1.2)	0.601
PPFx	35 (0.2)	1 (0.1)	1 (<0.1)	0 (0.0)	0.206
1-year Complications					
PJI	66 (0.3)	3 (0.2)	8 (0.2)	4 (0.7)	0.288
Aseptic Revision	2901 (12.5)	24 (2.0)	46 (1.3)	10 (1.7)	0.179
Aseptic Loosening	11 (0.01)	1 (0.1)	2 (0.1)	2 (0.3)	0.030
PPFx	59 (0.3)	3 (0.2)	3 (0.1)	1 (0.2)	0.270
2-year Complications					
PJI	79 (0.3)	5 (0.4)	10 (0.3)	5 (0.9)	0.175
Aseptic Revision	461 (0.2)	27 (2.2)	70 (2.0)	16 (2.7)	0.586
Aseptic Loosening	24 (0.1)	2 (0.2)	2 (0.1)	2 (0.3)	0.228
PPFx	75 (0.3)	3 (0.2)	7 (0.2)	2 (0.3)	0.629

PJI: Prosthetic Joint Infection; SSI: Surgical Site Infection; MUA: Manipulation Under Anesthesia; VTE: Venous Thromboembolism; PPFx: Peri-prosthetic Fracture

Table 3: Odds Ratio of Complications

	Denosumab		SERMs		Teriparatide	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
90-day Complications						
PJI	0.00	NaN	0.82	0.29-2.32	3.73	1.13-12.22
SSI	1.05	0.46-2.38	0.84	0.47-1.46	2.17	0.95-4.97
Aseptic Revision	2.11	1.22-3.66	1.29	0.84-1.98	1.56	0.64-3.80
MUA	0.85	0.57-1.27	0.81	0.63-1.03	0.63	0.33-1.22
Aseptic Loosening	0	NaN	0	NaN	6.61	0.80-54.79
VTE	0.79	0.46-1.36	1.13	0.85-1.50	0.82	0.39-1.74
PPFx	0.55	0.08-4.00	0.19	0.03-1.37	0.00	NaN
1-year Complications						
PJI	0.87	0.27-2.78	0.80	0.38-1.66	2.41	0.88-6.64
Aseptic Revision	1.54	1.02-2.32	1.01	0.74-1.38	1.33	0.71-2.48
Aseptic Loosening	1.74	0.23-13.52	1.19	0.26-5.39	7.23	1.60-32.68
PPFx	0.98	0.31-3.11	0.33	0.10-1.06	0.67	0.09-4.84
2-year Complications						
PJI	1.21	0.49-3.01	0.83	0.43-1.61	2.52	1.02-6.25
Aseptic Revision	1.13	0.76-1.67	0.997	0.77-1.29	1.39	0.84-2.30
Aseptic Loosening	1.60	0.38-6.78	0.55	0.13-2.32	3.31	0.78-14.04
PPFx	0.77	0.24-2.43	0.61	0.28-1.33	1.06	0.26-4.29

PJI: Prosthetic Joint Infection; SSI: Surgical Site Infection; MUA: Manipulation Under Anesthesia; VTE: Venous Thromboembolism ; PPFx: Peri-prosthetic Fracture