## Indications for Revision Total Knee Arthroplasty Among Hypertensive Patients Taking Thiazide Diuretics vs Loop Diuretics vs Combination Therapy

Jordan Villa, Jackson W. Durbin, Andrew Fealy, Philip M Parel, Emile Kuyl, Amil Raj Agarwal, Sabrina Gill, Alex Gu<sup>1</sup>, Robert S Sterling

<sup>1</sup>George Washington University School of Medicine An INTRODUCTION:

Loop diuretics and thiazide diuretics are common treatment options for patients with hypertension. Loop diuretics block the Na+/K+/2CI- cotransporter at the thick ascending loop of Henle in the kidney. Blocking this cotransporter subsequently inhibits the paracellular reabsorption of Ca2+ from the tubule, ultimately leading to increased urinary Ca2+ excretion. Increased urinary Ca2+ excretion can contribute to lower bone mineral density. Conversely, thiazide diuretics block the Na+/CI- symporter along the distal convoluted tubule in the loop of Henle. This leads to decreased intracellular concentration of Na+, which in turn increases Na+/Ca2+ exchange as well as Ca2+ reabsorption. Increasing Ca2+ reabsorption has been associated with increases in bone mineral density. Finally, combination therapy of loop and thiazide diuretics has been utilized for refractory fluid overload.

Much of the current literature has looked at the effect of thiazide and loop diuretics on bone mineral density. Additional research has looked at the effect of bone mineral density reducing drugs on outcomes and revision rates following total joint arthroplasty. No literature was identified that compared the indications for revision following total knee in hypertensive patients either taking loop diuretics, thiazide diuretics, or combination therapy.

METHODS: Patients who underwent primary TKA were identified using a national administrative claims database. Patients taking either thiazide diuretics, loop diuretics, or combination therapy were identified. Baseline demographics between the study cohorts were compared using Pearson chi-squared and student t-tests, where appropriate. Multivariate logistic regression analysis was utilized to observe significant differences in risk factors for 2-year all-cause revision, PPF, and mechanical loosening. Output was recorded as the odds ratios (OR), 95% confidence intervals (95% CI), and the p-value. A p-value less than 0.05 was used as the significance level for this study. All statistical analysis was conducted using R software (Vienna, Austria) provided by the PearlDiver database.

RESULTS: In total, 9,475 patients were identified that were taking thiazide diuretics, 110,231 that were taking loop diuretics, and 7,312 patients that were taking both thiazide and loop diuretics. 314,089 control patients were identified (Table 1). For the thiazide patients, loop patients, combination therapy patients, and control patients, the revision cumulative incidence rates were 1.74%, 2.56%, 2.22%, and 1.70%, respectively (Table 2). Patients taking loop diuretics experienced a higher rate of revision, periprosthetic fractures, and mechanical loosening than patients taking thiazide diuretics or combination therapy as compared to the control group (Table 2). Patients taking loop diuretics experienced higher revision when compared to control (OR: 1.3; 95% CI: 1.23-1.37; P = 0.006; Table 3).

DISCUSSION AND CONCLUSION: The findings suggest an increased risk of revision TKA for patients taking loop diuretics. This higher risk is likely associated with altered bone mineral density. The increased risk of revision highlights the importance of careful preoperative optimization and close postoperative monitoring in patients taking loop diuretics. Future research can identify targeted interventions to help mitigate the higher revision rates in this vulnerable population.

	Central		Thiazide Diazetics		LospI	Nurvtics	Com	erapy:	P-Value	
		14		94		**		96		
Total	441,107		9,475		110,231		7,912			
Sex (Male)	114,451	36.44%	4,750	50.15%	37,757	34.25%	3,139	42.93%	<0.001	
				Clinical C	cesochidi	ties				
Congestive Heart Failure	1,396	0.44%	637	6.72%	22,883	20.76%	7,312	14,70%	<0.001	
Artytaria	17,500	5.57%	1,817	29.18%	36,083	32.73%	1,851	25.31%	<0.001	
VkNular Disease	15,007	4.78%	1,670	17.63%	31,017	28.14%	1,660	22.70%	-0.001	
Polmenary Circulatory Disorder	3,853	1.29%	491	5.18%	12,833	11.64%	635	8.68%	~0.001	
Peripheni Vascular Disease	13,578	4.32%	2,896	22.12%	28,144	25.59%	1,943	26.57%	-0.001	
Obesity	50,372	16.04%	4,858	51.27%	52,699	47.81%	3,985	54,50%	-0.001	
Paralysia	1260	0.42%	129	1.36%	1,920	1.74%	110	1.50%	<0.001	
Neurologic Disease	6,484	2.06%	353	4.04%	6,479	5.85%	338	4.62%	<0.001	
Polynomary Disease	39,578	12.54%	2,564	27.06%	43,729	39.67%	2,485	33.99%	<0.001	
Disbetes Mellitus	37,320	11.88%	9,307	\$5.23%	59,655	54.12%	7,046	96.36%	<0.001	
10)pothyroidism	44,168	14.06%	2,431	25.66%	32,793	29.75%	2,058	28.56%	<0.001	
Chronic Kidney disease	4,141	1.32%	2,161	22.81%	25,491	23.13%	2,207	30.18%	-0.001	
Liver Disease	15,436	4915	1,441	15.21%	14,487	13.14%	1,041	14.24%	-10.001	
Puptic Ulcer Disease	4,913	1.59%	436	4.28%	5,753	5.22%	355	4.88%	-0.001	
Lynghoma	1,795	0.57%	501	1.07%	1,469	1.33%	89	1.22%	-00.001	

Cancer without Metastasis	24,055	7.66%	1,278	13.49%	15,949	14.47%	993	13.58%	<0.001
Rheamateid Arthritis/Collagen Disorder	10.002	3.18%	377	3.98%	7.230	6.56%	377	5.16%	<0.001
Coagedopativy	7,156	2.28%	559	5.90%	9,723	8.82%	548	7,49%	~0.001
Fluid and Electrolyte Disorder	16,215	5.38%	2,113	22.30%	34,260	31.08%	2,075	28.38%	<0.001
Anemia with Blood Loss	2,497	0.79%	294	3.10%	4,137	3.75%	267	3.65%	<0.001
Anexia without Blood Loss	13,678	435%	1,437	15.17%	18,164	15.45%	1,309	17.90%	<0.001
Alcohol Abase	4,763	1.52%	213	2.25%	4,363	3.78%	176	2.41%	<0.001
Drag Abase	6,543	2.08%	347	3.66%	6,217	5.64%	335	4.58%	<0.001
Prychosis	2,505	0.80%	195	2.06%	3,038	2.76%	186	2.54%	-0.001
Depression	52,223	16.63%	2,604	27.45%	34,059	30.90%	2,096	28.67%	<0.001
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Variable	Odds Ratio	95% Confidence Interval	P-Valo
Revision			
Thiazide Diaretics	0.85	0.75-0.95	<0.001
Loop Diamtics	13	1.23-1.37	0.006
Combination Therapy	0.93	0.83-1.04	<0.001
Peripeosthetic Fractures			
Thiazide Diaretics	1.55	1.16-2.06	<0.001
Loop Durstics	2.11	1.86-2.39	0.003
Combination Therapy	0.71	0.54-0.54	0.015
Mechanical Lossening			
Thiazide Diaretics	1.00	0.81-1.23	0.988
Loop Diamtics	1.28	1.17-1.40	<0.001