Delayed Administration of Apixaban Is Associated with Lower Bleeding Complications and Acute Anemia Without Increasing Thromboembolic Risk following Revision Total Knee Arthroplasty

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INTRODUCTION: Apixaban and rivaroxaban are effective prophylactic agents for prevention of venous thromboembolism (VTE) following revision total knee arthroplasty (TKA). However, optimal timing for starting these agents is controversial. This study sought to compare postoperative bleeding and thromboembolic complications among revision TKA patients starting postoperative apixaban or rivaroxaban on postoperative day (POD) 0 versus POD 1.

METHODS: A retrospective database including approximately 25% of all surgeries performed in the United States was queried from 2016 to 2023. Patients receiving apixaban or rivaroxaban on POD0 were compared to patients who received the same anticoagulant on POD1. Ninety-day postoperative bleeding complications (e.g. acute anemia, transfusion, hematoma, and hemorrhage) as well as thromboembolic complications (e.g. deep venous thrombosis (DVT), pulmonary embolism (PE), stroke and myocardial infarction) were compared between POD0 and POD1 for each medication. Multivariable regression was used to assess differences.

RESULTS: In total, 9,895 patients were identified, with 5,396 receiving apixaban (54.5%) and 4,499 receiving rivaroxaban (45.5%). Of patients receiving apixaban, 1,078 (20.0%) began anticoagulation on POD0 and 4,318 (80.0%) on POD1. Apixaban POD1 patients had a significantly decreased rate of aggregate bleeding complications (adjusted odds ratio [aOR]: 0.71, 95%-confidence interval (CI):0.50-1.00, p=0.047) and acute anemia (aOR: 0.67, 95%-CI:0.48-0.99, p=0.044). Of patients receiving rivaroxaban, 1,060 (23.6%) began anticoagulation on POD0 and 3,439 (76.4%) on POD1. Rivaroxaban POD1 patients had similar rates of bleeding complications relative to POD0 patients. Neither drug was associated with an increased risk of DVT or PE when administered on POD1 versus POD0.

DISCUSSION AND CONCLUSION:
For revision TKA patients, delaying administration of apixaban until POD1 was associated with reduced postoperative bleeding risk without increased risk of thromboembolic complications. Delayed administration of rivaroxaban led to no significant difference in bleeding and thrombotic complications; however, these findings were limited by smaller sample sizes in the rivaroxaban cohorts.

Table 1: Bleeding Complications

90-Day Postoperative Outcomes	Apixaban Day 0 (N= 1,078)		Apixaban Day 1 (N= 4,318)		Univariate Regression			Multivariable Regression		
	N	%	N	%	OR	95%-CI	P-Value	aOR	95%-CI	P-Value
Aggregate Bleeding Complications	48	4.5%	135	3.1%	0.69	(0.495 - 0.960)	**0.032**	0.71	(0.502 - 0.996)	**0.048**
Transfusion	13	1.2%	31	0.7%	0.59	(0.309 - 1.136)	0.115	0.67	(0.329 - 1.359)	0.266
Acute Anemia	37	3.4%	97	2.2%	0.65	(0.440 - 0.950)	**0.026**	0.67	(0.452 - 0.991)	**0.045**
Hematoma	6	0.6%	24	0.6%	1.00	(0.407 - 2.449)	0.998	1.00	(0.380 - 2.616)	0.995
Hemorrhage	4	0.4%	14	0.3%	0.87	(0.287 - 2.659)	0.812	0.83	(0.266 - 2.616)	0.755

Table 2: Thromboembolic Complications

90-Day Postoperative Outcomes	Apixaban Day 0 (N= 1,078)		Apixaban Day 1 (N= 4,318)		Univariate Regression			Multivariate Regression		
	N	%	N	%	OR	95%-CI	P-Value	aOR	95%-CI	P-Value
Deep Vein Thrombosis	4	0.4%	30	0.7%	1.88	(0.660 - 5.344)	0.237	2.18	(0.823 - 5.765)	0.117
Pulmonary Embolism	4	0.4%	14	0.3%	0.87	(0.287 - 2.659)	0.812	0.95	(0.303 - 2.932)	0.924
Stroke	1	0.1%	3	0.1%	0.75	(0.078 - 7.207)	0.802	N/A	N/A	N/A
Myocardial Infarction	2	0.2%	9	0.2%	1.12	(0.242 - 5.209)	0.882	1.57	(0.197 - 12.473)	0.672

Table 3: Bleeding Complications

90-Day Postoperative Outcomes	Rivaroxaban Day 0 (N= 1,060)		Rivaroxaban Day 1 (N= 3,439)		Univariate Regression			Multivariable Regression		
	N	%	N	%	OR	95%-CI	P-Value	aOR	95%-CI	P-Value
Aggregate Bleeding Complications	36	3.4%	100	2.9%	0.85	(0.578 - 1.255)	0.417	0.86	(0.576 - 1.285)	0.462
Transfusion	9	0.8%	24	0.7%	0.82	(0.380 - 1.771)	0.615	0.76	(0.322 - 1.795)	0.532
Acute Anemia	22	2.1%	62	1.8%	0.87	(0.530 - 1.416)	0.567	0.79	(0.475 - 1.308)	0.357
Hematoma	4	0.4%	20	0.6%	1.54	(0.527 - 4.529)	0.429	1.95	(0.699 - 5.429)	0.202
Hemorrhage	7	0.7%	20	0.6%	0.88	(0.371 - 2.087)	0.772	1.00	(0.402 - 2.491)	0.999

Table 4: Thromboembolic Complications

90-Day Postoperative Outcomes	Rivaroxaban Day 0 (N= 1,060)		Rivaroxaban Day 1 (N= 3,439)		Univariate Regression			Multivariate Regression		
	N	%	N	%	OR	95%-CI	P-Value	aOR	95%-CI	P-Value
Deep Vein Thrombosis	6	0.6%	16	0.5%	0.82	(0.320 - 2.104)	0.681	0.84	(0.299 - 2.366)	0.743
Pulmonary Embolism	6	0.6%	13	0.4%	0.67	(0.253 - 1.758)	0.412	0.72	(0.240 - 2.153)	0.556
Stroke	2	0.2%	6	0.2%	0.92	(0.186 - 4.588)	0.924	1.01	(0.307 - 3.290)	0.992
Myocardial Infarction	3	0.3%	3	0.1%	0.31	(0.062 - 1.527)	0.149	0.22	(0.031 - 1.618)	0.138