

Low Molecular Weight Heparin Prophylaxis is Associated with Lower Rates of Venous Thromboembolism when Compared to Direct Oral Anticoagulants in Patients Undergoing Surgical Resection for Primary Lower Extremity Soft-Tissue Sarcoma

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INTRODUCTION: Malignancy-induced hypercoagulability represents a significant cause of morbidity and mortality. Limited data exists regarding the efficacy and safety of direct oral anticoagulants (DOAC) vs. low-molecular-weight heparin (LMWH) for postoperative venous thromboembolism (VTE) prophylaxis after surgical resection in sarcomas. We aimed to assess the efficacy and safety of DOACS and LMWH for VTE prophylaxis in patients after surgical resection of primary lower extremity soft-tissue sarcomas (LE-STs).

METHODS: We conducted a retrospective, cohort analysis using a large insurance database. We identified 2,459 patients undergoing surgical resection of primary LE-STs with greater than or equal to 90-days follow up. Of these patients, 13% (321) received DOACs and 28% (690) received LMWH prophylaxis. We compared efficacy and safety of VTE prophylaxis via incidence and odds of deep venous thrombosis (DVT), pulmonary embolism (PE), postoperative anemia, bleeding complications, and blood transfusions within 90 days postoperatively. Univariate and multivariable analysis was conducted to assess significant differences in complications between VTE prophylaxis modalities.

RESULTS: The incidence of DVT (15%) and PE (10%) were higher in DOACs when compared to the LMWH cohort (10% and 4.5%, respectively). DOACs had higher odds of DVT (OR: 1.7; 95% CI: [1.1-2.5], $p=0.016$) and PE (OR: 2.6; 95% CI: [1.5-4.5], $p<0.001$) when compared to LMWH after controlling for confounders. There were no differences in the incidence and odds of postoperative anemia, bleeding complications, or blood transfusions.

DISCUSSION AND CONCLUSION: There were higher incidences and odds of PE and DVT, but not bleeding complications, in patients receiving DOACs for VTE prophylaxis after surgical resection of primary LE-STs. These findings suggest that LMWH may be a more favorable option than DOACs in the LE-STs patient population. Further studies investigating the efficacy of DOACs in malignancy-induced hypercoagulability postoperatively are required.

Table 1. Demographic and Comorbidity of Patients Undergoing Surgical Resection for Lower Extremity Soft-Tissue Sarcoma

	Total N	Direct Oral Anticoagulants		Low Molecular Weight Heparin		p-value ¹
		N	%	N	%	
Total	1011	321		690		
Age (Mean \pm SD)	-	64.1 \pm 13.9		55.8 \pm 15.6		<0.001
Gender						0.015
Male	518	183	35.3%	335	48.55%	
Female	493	138	27.99%	355	51.45%	
Comorbidity						
CHF	34	10	3.12%	24	3.48%	0.912
Arrhythmias	99	28	8.72%	71	10.29%	0.505
Valvular Disease	50	15	4.67%	35	5.07%	0.907
Pulmonary Circulation Disorders	23	6	1.87%	17	2.46%	0.716
PVD	46	13	4.05%	33	4.78%	0.72
Hypertension	117	28	8.72%	89	12.90%	0.068
Paralysis	6	3	0.93%	3	0.43%	0.999
Other Neurological Disorders	10	4	1.25%	6	0.87%	0.824
CPD	54	14	4.36%	40	5.80%	0.427
Diabetes Mellitus	47	12	3.74%	35	5.07%	0.437
Hypothyroidism	40	9	2.80%	31	4.49%	0.267
Chronic Kidney Disease	38	13	4.05%	25	3.62%	0.877
Liver Disease	49	9	2.80%	40	5.80%	0.057
Peptic Ulcer Disease	3	0	0.00%	3	0.43%	0.574
Rheumatoid Arthritis and Collagen Disease	13	2	0.62%	11	1.59%	0.329
Congestive Heart Failure	38	7	2.18%	31	4.49%	0.105
Fluid and Electrolyte Disorders	80	15	4.67%	65	9.42%	0.013
Blood Loss Anemia	11	2	0.62%	9	1.30%	0.518
Deficiency Anemia	32	8	2.49%	24	3.48%	0.322
Alcohol Abuse	0	0	0.00%	0	0.00%	0.999
Drug Abuse	10	2	0.62%	8	1.16%	0.645
Psychoses	3	0	0.00%	3	0.43%	0.574
Depression	52	10	3.12%	42	6.09%	0.066
Smoking	21	3	0.93%	18	2.61%	0.133
Obesity	52	15	4.67%	37	5.36%	0.757

SD, standard deviation; CHF, congestive heart failure; PVD, peripheral vascular disease; CPD, chronic pulmonary disease
¹ Pearson's chi-squared test

Table 2. Univariate and Multivariable 90-Day Complications following Surgical Resection for Lower Extremity Soft-Tissue Sarcoma

	Univariate ¹						Multivariable ²		
	Total DOAC			LMWH			DOAC vs. LMWH		
	N	%	p-value	N	%	p-value	OR	95% CI	p-value
DVT	117	49	15.26%	68	9.86%	0.016	1.65	[1.09-2.49]	0.016
PE	62	31	9.66%	31	4.49%	0.002	2.62	[1.52-4.54]	<0.001
Post-operative Anemia	71	24	7.48%	47	6.81%	0.800	1.18	[0.69-1.99]	0.542
Bleeding Complications	44	13	4.05%	31	4.49%	0.876	0.98	[0.50-1.95]	0.958
Blood Transfusions	47	12	3.74%	35	5.07%	0.437	0.88	[0.44-1.79]	0.730

DOAC, direct oral anticoagulant; LMWH, low molecular weight heparin; OR, odds ratio; DVT, deep venous thrombosis; PE, pulmonary embolism

¹ Pearson's chi-squared test
² Multivariable logistic regression adjusting for age, biological sex, and significantly different baseline comorbidities with $p<0.05$ on univariate analysis

Figure 1. 90-Day Postoperative Incidence Rates of Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE) after Lower Extremity Soft Tissue Sarcoma Resection

