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Blood 142 (2023) 2642–2644

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

332.THROMBOSIS AND ANTICOAGULATION: CLINICAL AND EPIDEMIOLOGICAL

Predictors and Timing of Venous Thromboembolism in Lymphoma

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Introduction

Cancer associated thrombosis (CAT) is common in lymphoma, but the risk is not well characterized. While prophylactic anticoagulation is recommended in certain solid tumors, routine prophylaxis is not practiced in hematologic malignancies. The Kohrana CAT risk score considers lymphoma a single entity. We aimed to identify the incidence rate of venous thromboembolism (VTE) and risk factors in lymphoma patients at our institution.

Methods

Patients diagnosed with lymphoma between 2018 and 2022 were identified through our institution's tumor registry. Using automated text search from our electronic medical record (EPIC®) combined with natural language processing review, VTE events were identified from 90 days before and up to one year(y) after initiation of chemotherapy initiation, or diagnosis date if no chemotherapy was administered. VTE events included lower extremity deep vein thrombosis (DVT) or pulmonary embolism (PE). Events were reviewed and adjudicated manually by us. We report time to event analysis and survival analysis using Kaplan-Meier curve. The study was censored at one year. Univariate and multivariate analyses were performed using COX-regression model. We evaluated the effect of indolent versus aggressive lymphoma, stage, age, sex, race, ethnicity, white blood cell count, hemoglobin, and platelet count.

Results

We identified 879 patients(pts) with lymphoma; of those, 378 pts had indolent lymphoma (I-Lym) and 501 pts had aggressive lymphoma (A-Lym). Median age was 61y. 464 pts (52.8%) were above 60 y, 477 pts (54.3%) were males, and 325 pts (37.0%) were Hispanic. Race was distributed as follows: 89.5% white, 9.1% Black, and 1.4% other. 56.9% had advanced stage lymphoma. VTE occurred in 4.9% (n=43) of the overall population within 12 months. The incidence was higher in A-Lym (7.2%, n=36) compared with I-Lym (1.9%, n=7), $p<0.001$. For both A-Lym and I-Lym, 32.6% of the VTE events occurred prior to diagnosis or initiation of chemotherapy. Among patients who developed thrombosis after the chemotherapy start date, the median time to thrombosis was 39 days.

In a univariate analysis (Table 1) for thrombosis-free survival, age>60, receiving chemotherapy and A-Lym, were all associated with higher risk of thrombosis ($p<0.05$). In the multivariate analysis, only, age>60, and A-Lym remained significant in predicting thrombosis (HR: 3.48, 95%CI: 1.41, 8.61, p=0.007). Hemoglobin <10, platelet count >350, white blood cell count >11, advanced stage, and chemotherapy administration were not significant risks of thrombosis.

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In multivariate analysis for overall survival (Table 2), development of VTE was associated with increased risk of mortality (HR: 2.59, 95%CI: 1.38, 4.87, p=0.003). This relationship of VTE and mortality was observed independently in both I-Lym and A-Lym. As expected, A-Lym, age>60, male sex, and advanced stage all predicted worse survival in our lymphoma population ($p<0.05$ for all). Of note, hemoglobin <10 and white blood cell count >11, did not predict VTE in lymphoma but did predict poor OS.

Conclusion

Lymphoma is associated with a clinically relevant rate of CAT, but incidence is significantly higher in A-Lym compared with I-Lym with a third of events occurring prior to chemotherapy. The hematologic parameters of the Khorana Score (WBC, Hgb, platelet count) did not correlate with incidence of CAT in lymphoma, neither did chemotherapy. Development of CAT during therapy, in multivariate analysis for both A-Lym and I-Lym, was associated with a marked reduction in OS. These points suggest that the thrombotic risk is an inherent property of lymphoma biology in at least some cases, leading to an increased risk of CAT as well as reduced OS. We do not propose that CAT-related mortality is driving the reduced OS, but more likely a marker of poorer prognosis.

Limitations:

This was a single center/ single dataset and these findings should be considered a derivation cohort, and should be verified with independent additional datasets. If our findings are verified, prospective studies to assess benefit of prophylactic anticoagulation in aggressive lymphoma may be warranted.

Disclosures Trabolsi: *Johnson & Johnson:* Current equity holder in publicly-traded company. **Kronenfeld:** *Bayer Healthcare Pharmaceuticals:* Research Funding. **Caballero:** *Microsoft Corp:* Current equity holder in publicly-traded company; *Organon & Co:* Current equity holder in publicly-traded company; *Exact Sciences Corp:* Current equity holder in publicly-traded company; *Merck And Co Inc:* Current equity holder in publicly-traded company. **Lossos:** *LRF:* Membership on an entity's Board of Directors or advisory committees; *Adaptive:* Honoraria; *NCI:* Research Funding; *NCI:* Research Funding; *University of Miami:* Current Employment; *BeiGene:* Consultancy. **Soff:** *Anthos Therapeutics:* Research Funding; *Sanofi:* Consultancy.

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Table1. Risk Factors for Venous Thromboembolism

		UVA		MVA	
Variable	Category	HR (95% CI)	p	HR (95% CI)	p
Age	<60	Ref		Ref	
	>=60	2.41 (1.33, 4.75)	0.010	2.75 (1.40, 5.37)	0.003
Sex	Female	Ref		NA	
	Male	0.55 (0.30, 1.02)	0.058		
Race	White	Ref		NA	
	Black	1.62 (0.68, 3.84)	0.273		
	Other/Unknown	NE			
Hispanic	Non-Hispanic	Ref		NA	
	Hispanic	1.38 (0.75, 2.53)	0.302		
	Unknown	1.77 (0.24, 13.12)	0.575		
Stage	I-II	Ref		Ref	
	III-IV	2.14 (0.94, 4.86)	0.071	2.21 (0.97, 5.03)	0.06
	Unknown	1.57 (0.53, 4.67)	0.417	1.68 (0.56, 5.06)	0.356
Lymphoma category	Indolent	Ref		Ref	
	Aggressive	4.05 (1.80, 9.10)	<.001	3.48 (1.41, 8.61)	0.007
Hemoglobin (gm/dL)	<10	Ref		NA	
	>=10	1.09 (0.58, 2.05)	0.777		
Platelet count (X 10^9/L)	<350	Ref		NA	
	>=350	0.74 (0.26, 2.06)	0.559		
White blood cells (X 10^9/L)	<11	Ref		NA	
	>=11	0.92 (0.41, 2.07)	0.845		
Chemotherapy	No	Ref		Ref	
	Yes	3.67 (1.31, 10.28)	0.013	1.93 (0.60, 6.15)	0.268

Table 2. Predictors of Overall Survival

		UVA		MVA	
Variable	Category	HR (95% CI)	p	HR (95% CI)	p
Age	<60	Ref		Ref	
	>=60	2.77 (1.67, 4.61)	<.001	2.95 (1.74, 5.00)	<.001
Sex	Female	Ref		Ref	
	Male	1.66 (1.04, 2.65)	0.033	1.79 (1.12, 2.88)	0.015
Race	White	Ref		Ref	
	Black	1.91 (1.03, 3.53)	0.040	1.37 (0.71, 2.62)	0.350
	Other/Unknown	1.15 (0.16, 8.31)	0.888	1.84 (0.25, 13.43)	0.546
Hispanic	Non-Hispanic	Ref		NA	
	Hispanic	1.08 (0.69, 1.70)	0.743		
	Unknown	NE			
AJCC stage	I II	Ref		Ref	
	III-IV	7.20 (2.61, 19.85)	<.001	5.50 (1.97, 15.31)	0.001
	Unknown	8.04 (2.71, 23.90)	<.001	6.40 (2.14, 19.17)	<.001
Lymphoma category	Indolent	Ref		Ref	
	Aggressive	3.31 (1.89, 5.82)	<.001	3.83 (2.16, 6.80)	<.001
Hemoglobin (gm/dL)	<10	Ref		Ref	
	>=10	0.43 (0.28, 0.68)	<.001	0.43 (0.27, 0.69)	<.001
Platelet count (X 10^9/L)	<350	Ref		NA	
	>=350	0.82 (0.39, 1.70)	0.591		
White blood cells (X 10^9/L)	<11	Ref		Ref	
	>=11	2.02 (1.24, 3.29)	0.005	2.31 (1.41, 3.78)	<.001
Chemotherapy	No	Ref		NA	
	Yes	1.03 (0.62, 1.72)	0.904		
Thrombosis (TB)	No	Ref		Ref	
	Yes	4.77 (2.67, 8.50)	<.001	2.59 (1.38, 4.87)	0.003

NE: not estimable, NA: not applicable. > Aggressive lymphoma includes; large B cell lymphoma (61.82%), Hodgkin lymphoma (23.03%), T cell lymphoma (10.65%), Burkitt lymphoma (2.47%), other (2.03%). > Indolent lymphoma includes; follicular lymphoma (35.78%), chronic lymphocytic lymphoma/leukemia (22.02%), marginal zone lymphoma (19.63%), mantle cell lymphoma (12.29%), lymphoplasmacytic lymphoma (1.47%), other (8.81%).

Figure 1

https://doi.org/10.1182/blood-2023-173903

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