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P1062 A REAL-WORLD EVALUATION OF THE ASSOCIATION BETWEEN ELEVATED BLOOD COUNTS AND THROMBOTIC EVENTS IN POLYCYTHEMIA VERA: AN ANALYSIS OF DATA FROM THE REVEAL STUDY

Topic: 16. Myeloproliferative neoplasms - Clinical

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Background: Polycythemia vera (PV) is characterized by clonal hematopoiesis leading to elevated peripheral blood counts and an increased risk of thrombotic events (TEs). Advanced age and TE history form the conventional risk model used to determine TE risk/treatment strategy. Associations between TEs and elevated hematocrit (HCT) levels exist, but associations with white blood cell (WBC) or platelet (PLT) counts have not been assessed consistently. The large, real-world, prospective Observational Study of Pts with Polycythemia Vera in US Clinical Practices (REVEAL; NCT02252159) followed pts with PV treated in community or academic centers.

Aims: This analysis evaluated associations between elevated blood counts and TEs in pts with PV using data from REVEAL.

Methods: Eligible pts had ≥3 lab values (blood counts) post-enrollment; pts with a post-enrollment TE but no lab value <6 mo before that TE were excluded. The association between blood counts and TEs was assessed using a time-dependent covariate Cox proportional hazards model. Time to first post-enrollment TE was modeled with time censored at last known visit for pts with no TE. Each lab parameter was modeled with sex, age, disease duration, and TE history at enrollment as baseline covariates and treatment as a time-dependent covariate. Blood counts were included as binary time–dependent covariates using the following thresholds: HCT >45%, WBC >11×10^9/L, PLT >400×10^9/L. Linear interpolation was used to determine lab values between observed lab values. Alternative thresholds for WBC (<7, ≥7 to <8.5; ≥8.5 to <11, and ≥11×10^9/L, and >12×10^9/L with HCT controlled at ≤45%) and PLT counts (>600×10^9/L) were evaluated. Statistical significance was considered at P<0.05.

Results: 2271/2510 pts were eligible (median age, 66 y [range, 22–95]; male, 54.1%). Median disease duration was 4.1 y (range, 0–56.3), 456 (20.1%) had TE history; 52.6% of pts received hydroxyurea. Of 106 pts who had TEs, 30 had arterial TEs (most commonly, transient ischemic attack [n=15]) and 76 had venous TEs (most commonly, deep vein thrombosis [n=37]).

Elevated HCT levels (>45%, hazard ratio [HR]=1.84 [95% CI, 1.234–2.749], P=0.0028), WBC (>11×10^9/L, HR=2.35 [1.598–3.465], P<0.0001), and PLT counts (>400×10^9/L, HR=1.60 [1.088–2.359], P=0.0170) were each associated with increased TE risk (**Table 1**). WBC count ≥11×10^9/L is associated with the highest TE risk compared with WBC count <7×10^9/L (HR=2.61 [95% CI, 1.594–4.262], P<0.0001). Elevated WBC >12×10^9/L was significantly associated with increased risk of TE with HCT controlled at ≤45%. PLT count (>600×10^9/L) increased TE risk (HR=1.37 [95% CI, 0.763–2.468]) compared with PLT count ≤600×10^9/L, but this was not statistically significant (P>0.05). In all models, advanced age, female sex, and TE history were associated with increased TE risk.

Image:

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Table 1. Association Between Blood Count Values and TEs

Analysis	HR (95% CI)	*P* Value
Association between elevated HCT and TEs		
Age, y	1.03 (1.01–1.046)	0.0026
Male sex (M vs F)	0.54 (0.362–0.799)	0.0021
Disease duration, y	0.98 (0.952–1.017)	0.3438
History of TE (Y vs N)	2.49 (1.667–3.717)	<0.0001
Treatment (HU vs none)	0.95 (0.626–1.435)	0.8004
Treatment (any other vs none)	0.78 (0.39–1.577)	0.4951
HCT (>45% vs ≤45%)	1.84 (1.234–2.749)	0.0028
Association between elevated WBC count and TEs		
Age, y	1.02 (1.007–1.042)	0.0068
Male sex (M vs F)	0.58 (0.393–0.858)	0.0063
Disease duration, y	0.98 (0.947–1.014)	0.2488
History of TE (Y vs N)	2.42 (1.623–3.619)	<0.0001
Treatment (HU vs none)	0.98 (0.651–1.486)	0.9386
Treatment (any other vs none)	0.67 (0.335–1.325)	0.2468
WBC (>11 vs ≤11)	2.35 (1.593–3.465)	<0.0001
Association between elevated PLT count (>400) and TEs		
Age, y	1.03 (1.01–1.046)	0.0022
Male sex (M vs F)	0.62 (0.416–0.914)	0.0162
Disease duration, y	0.99 (0.953–1.019)	0.3901
History of TE (Y vs N)	2.45 (1.64–3.654)	<0.0001
Treatment (HU vs none)	0.87 (0.58–1.319)	0.5223
Treatment (any other vs none)	0.66 (0.334–1.324)	0.2456
PLT (>400 vs ≤400)	1.60 (1.088–2.359)	0.0170
Association between elevated WBC count and TEs (4 WBC levels (<7, ≥7 to <8.5, ≥8.5 to <11, and ≥11)		
Age, y	1.02 (1.006–1.042)	0.0076
Male sex (M vs F)	0.59 (0.396–0.865)	0.0071
Disease duration, y	0.98 (0.948–1.015)	0.2646
History of TE (Y vs N)	2.42 (1.618–3.608)	<0.0001
Treatment (HU vs none)	1.00 (0.66–1.509)	0.9932
Treatment (any other vs none)	0.67 (0.336–1.328)	0.2496
WBC (≥7 to <8.5 vs <7)	1.01 (0.504–2.022)	0.9778
WBC (≤8.5 to <11 vs <7)	1.40 (0.76–2.595)	0.2790
WBC (≥11 vs <7)	2.61 (1.594–4.262)	0.0001
Association between elevated PLT count (>600) and TEs		
Age, y	1.03 (1.01–1.046)	0.0019
Male sex (M vs F)	0.59 (0.398–0.872)	0.0081
Disease duration, y	0.98 (0.951–1.017)	0.3316
History of TE (Y vs N)	2.43 (1.627–3.626)	<0.0001
Treatment (HU vs none)	0.89 (0.585–1.34)	0.5657
Treatment (any other vs none)	0.67 (0.335–1.331)	0.2517
PLTs (>600 vs ≤600)	1.37 (0.763–2.468)	0.2913
Association between elevated WBC count and TEs at HCT levels ≤45% (WBC >11 and >12)*		
WBC (>11 vs ≤11 × 10^9/L at HCT ≤45%)	1.81 (0.993–3.301)	0.0526
WBC (>12 vs ≤12 × 10^9/L at HCT ≤45%)	1.95 (1.066–3.554)	0.0300

Significant values are indicated in bold/blue font. Lab values are expressed as ×10^9/L. *Age, sex, disease duration, history of TE, HU usage, other treatments, WBC, HCT, and the interaction of WBC and HCT were used in the model to calculate the HR (95% CI). Treatment and categorical blood counts were included as time-dependent covariates in the models. Other treatments include interferon, busulfan, chlorambucil, anagrelide, and ruxolitinib. CI, confidence interval; HCT, hematocrit; HR, hazard ratio; HU, hydroxyurea; PLT, platelet; TE, thrombotic event; WBC, white blood cell.

Summary/Conclusion: This analysis of REVEAL, the largest real-world cohort of PV pts to date, demonstrated that elevated HCT levels (>45%), WBC (>11×10^9/L), and PLT counts (>400×10^9/L) were associated with increased TE risk. An association of elevated WBC >12×10^9/L with increased risk of TE was also observed when HCT was controlled, indicating that TE risk may be reduced by controlling WBC as well as HCT. These data support the need to incorporate blood count into risk stratification and treatment strategies for pts with PV in clinical practice and to move beyond the conventional risk model. Further studies to understand the causal relationship between elevated blood counts and TEs are warranted.

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