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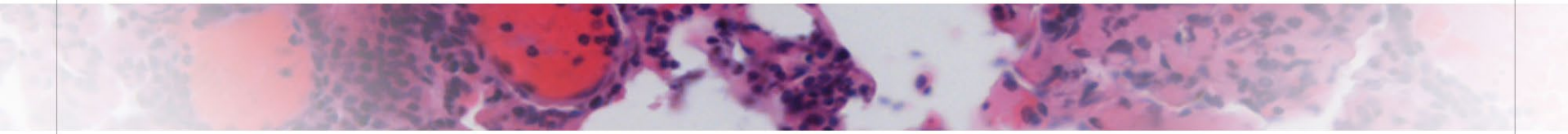

Real-World Analysis of Thromboembolic Event Rates in Patients in the United States with Polycythemia Vera

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Introduction

- Polycythemia Vera (PV) is a myeloproliferative neoplasm associated with an increased risk of thromboembolic events (TEs)
  - Patients with PV are characterized based on their risk for TEs as low-risk (age <60 without prior history of TE) or high-risk (age ≥60 and/or prior history of TE)
- Observational studies have shown higher rates of TEs in PV patients compared to matched controls (14.3 vs 4.9/1000 patient years [PY]), with proportions as high as 40% in patients with PV[1-3]
- We assessed the rate of arterial and venous TEs in a large cohort of low- and high-risk PV patients

PV, polycythemia vera; TE, thromboembolic event.

1. Goyal RK, et al. *Blood*. 2014;124:4840. 2. Griesshammer M, et al. *Ann Hematol*. 2019;98:1071-82. 3. Pemmaraju N, et al. *Leuk Res*. 2022;115:106809.

Methodology

- The Optum® MarketClarity Database contains HIPAA-compliant, de-identified data from a cumulative population of >105 million patients in the United States, including those with all insurance types and those who are uninsured
- For inclusion in this analysis, patients were required to have >1 year of electronic health records (EHR) data preceding the first diagnosis of PV ("index date") and >1 year of post-index EHR data or death prior to data period end (Data period: 1/1/2007 - 12/31/2019)
- Patients were stratified into three groups based on risk status at index: low-risk (age <60 without prior history of TE), age-based high-risk (age ≥60 without prior history of TE) and event-based high-risk (prior history of TE)
- TE outcomes were identified at the first occurrence of a diagnosis code for a TE in EHR during the post-index period

EHR, electronic health record; HIPAA, Health Insurance Portability and Accountability Act; PV, polycythemia vera; TE, thromboembolic event.

Methodology (continued)

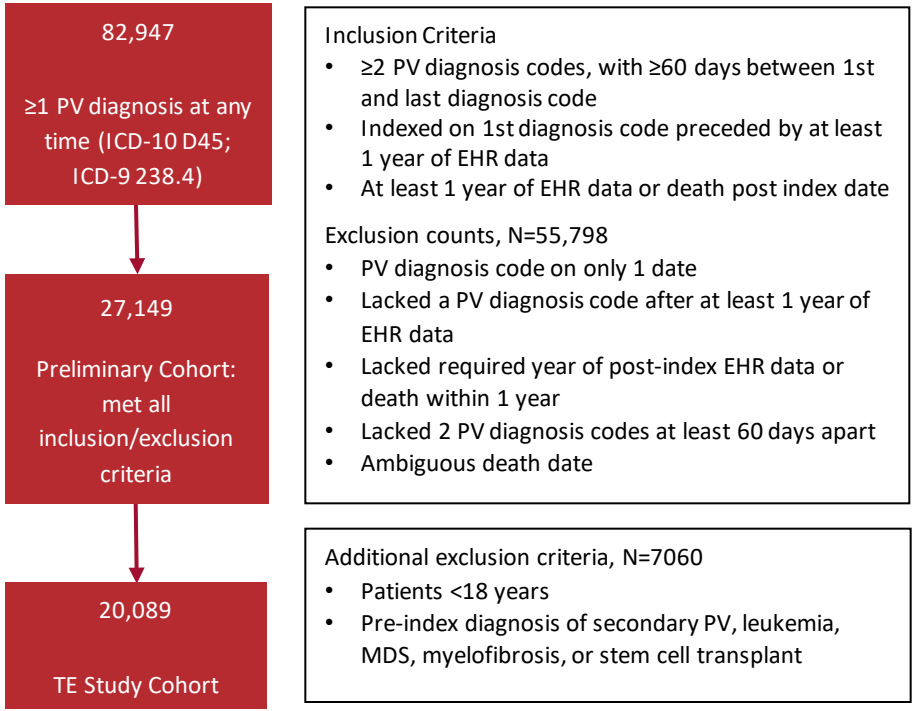
- All-cause mortality was identified through linked social security records with death dates provided by data vendor
- Descriptive statistics were used to characterize the proportion of patients with TEs
- Kaplan-Meier analysis was used to evaluate TE-free survival and overall survival among patients in the three risk groups at various time points. Patients were censored at death or last engagement date
- Cox Proportional Hazards models were used to evaluate predictors of TEs and mortality
- Covariates included clinical and demographic information including age, sex, race, region, comorbid or pre-existing medical conditions and laboratory values
- P-values were not adjusted for multiplicity

PY, patient-years; TE, thromboembolic event.

Baseline Characteristics and Demographics

- 20,089 patients with PV qualified for this retrospective study (mean age, 63.0 years; 57.8% male; 88.6% Caucasian)
  - Median duration of follow-up was 4.3 years (IQR, 2.4-5.9)
  - 16.2% (N=3256) were classified as event-based high-risk, 49.4% (N=9924) were age-based high-risk, and approximately one-third (34.4%; N=6909) were low-risk

Figure 1. Patient Population



EHR, electronic health record; IQR, interquartile range; MDS, myelodysplastic syndromes; PV, polycythemia vera; TE, thromboembolic event.

Post-Index TE

- Overall, 25.1% (5035/20,089) of patients with PV experienced at least one TE during the post-index period (**Table 1**)
  - TE incidence was highest among event-based high-risk patients (50.2%; 1634/3256), followed by age-based high-risk (25.0%; 2480/9924) and low-risk patients (13.3%; 921/6909)
    - Patients classified as event-based high risk had the highest frequency of TE for both venous and arterial events
  - The most common arterial events were stroke (7.1%) and MI/ACS (6.4%)
  - The most common venous events were DVT/deep thrombophlebitis (8.1%) and pulmonary embolism (4.5%)

Table 1. Percentage of Patients with a Post-Index TE, by Risk Status and Type of Event

Parameters	Total cohort	Event-based high-risk	Age-based high-risk	Low-risk
Total	N=20,089	*n*=3256	*n*=9924	*n*=6909
Any TE[1], *n* (%)	5035 (25.1)	1634 (50.2)	2480 (25.0)	921 (13.3)
Venous events, *n* (%)				
DVT/deep thrombophlebitis	1629 (8.1)	570 (17.5)	759 (7.6)	300 (4.3)
Pulmonary embolism	910 (4.5)	372 (11.4)	388 (3.9)	150 (2.2)
Superficial thrombophlebitis	154 (0.8)[2]	51 (1.6)	75 (0.8)	28 (0.4)
Arterial events, *n* (%)				
Stroke	1430 (7.1)	472 (14.5)	755 (7.6)	203 (2.9)
MI/ACS	1281 (6.4)	384 (11.8)	677 (6.8)	220 (3.2)
Transient ischemic attack	960 (4.8)	327 (10.0)	496 (5.0)	137 (2.0)
Peripheral arterial thrombosis	486 (2.4)	184 (5.7)	199 (2.0)	103 (1.5)

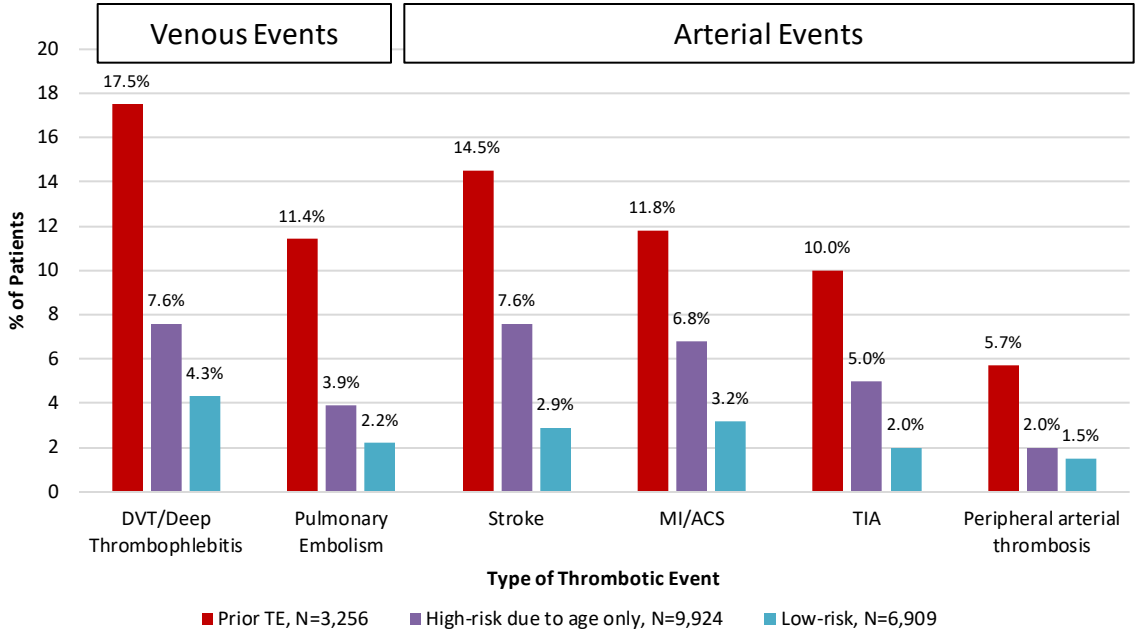
TEs outcomes were identified at the first occurrence of a diagnosis code for a TE.
[1]Any TE was assessed separately and includes all listed event categories plus abdominal thrombosis, Budd-Chiari syndrome, deep vein thrombosis (DVT), myocardial infarction (MI), acute coronary syndrome (ACS), peripheral arterial thrombosis, portal vein thrombosis, pulmonary embolism, stroke, transient ischemic attack (TIA), thrombophlebitis, and over 75 diagnostic codes for other thrombosis such as retinal artery occlusion and retinal vein occlusion, but is smaller than the sum of the individual categories shown.
[2]Of the 154 patients with superficial thrombophlebitis outcomes, 101 also had a DVT/thrombophlebitis diagnosis or events not considered superficial.

ACS, acute coronary syndrome; DVT, deep vein thrombosis; MI, myocardial infarction; PV, polycythemia vera; TE, thromboembolic event.

Post-Index TE (continued)

- Across all major categories of TE, whether venous or arterial, patients with prior TE had roughly double the proportions of TE events compared with patients classified as high-risk on age alone, and over triple the proportion compared to patients classified as low-risk

Figure 2. Percent of Patients with a Post-Index TE, by Risk Group and Type of Event

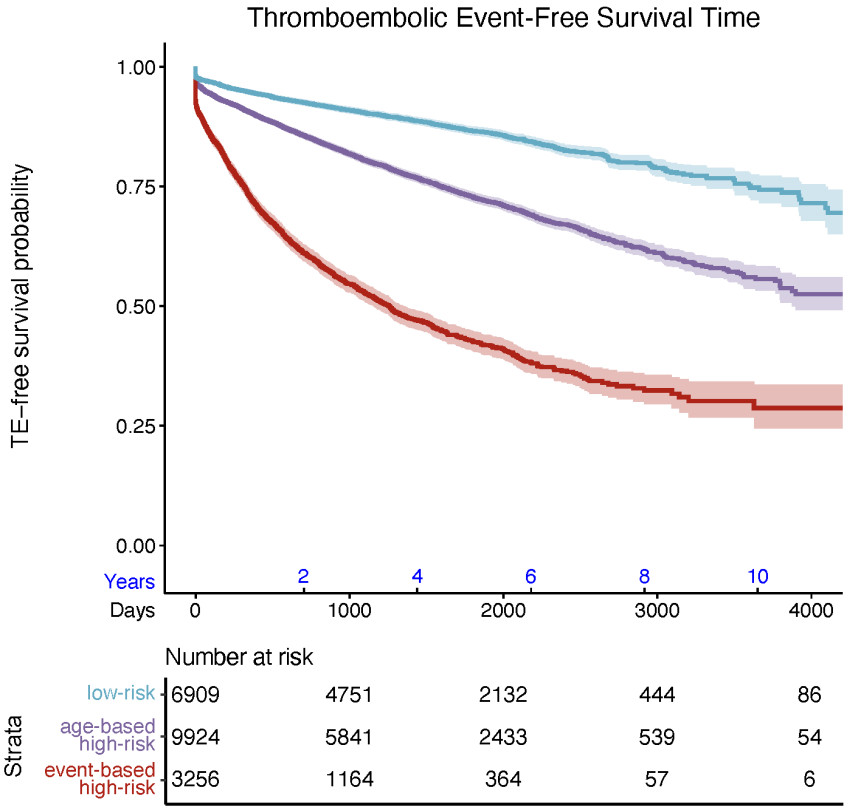


ACS, acute coronary syndrome; DVT, deep vein thrombosis; MI, myocardial infarction; TE, thromboembolic event; TIA, transient ischemic attack.

Probability of TE Event-Free Survival

- At approximately 2.5 years post-index, TE-free survival was ≈90% for low-risk, ≈80% for age-based high-risk, and ≈55% for event-based high-risk patients (**Figure 3**)
- At approximately 5.5 years post-index, TE-free survival had fallen to ≈85% for low-risk, ≈70% for age-based high-risk, and ≈40% for event-based high-risk patients
- The downward trend continued until the end of the data period

Figure 3. Kaplan-Meier Analysis Evaluating Probability of TE Event-Free Survival

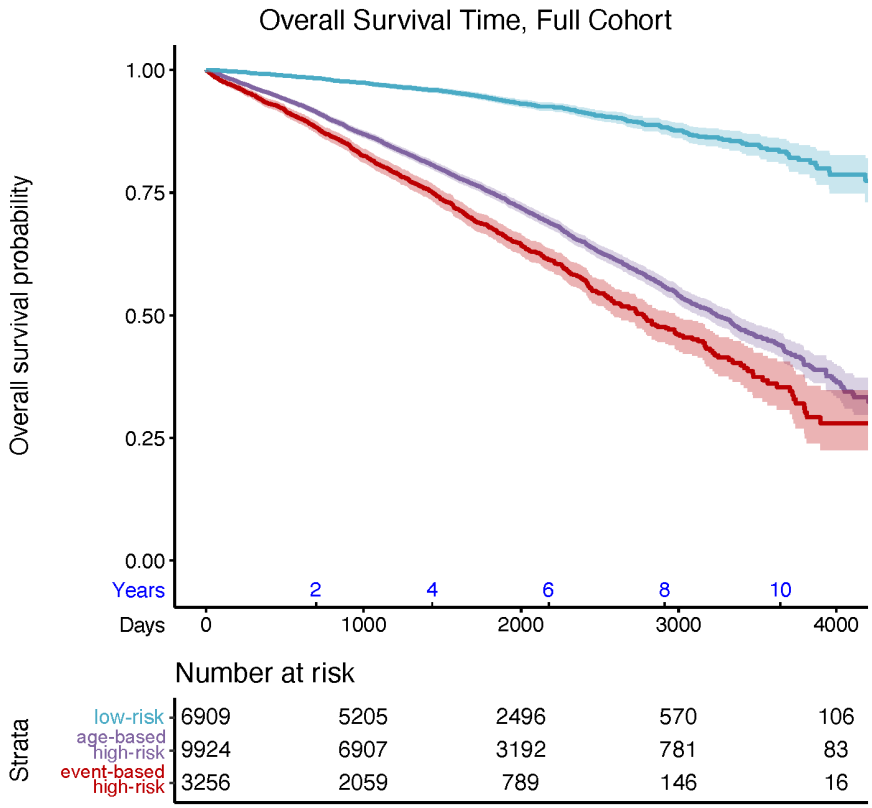


TE, thromboembolic event.
Kaplan-Meier TE-free survival curves with 95% confidence interval for each risk group within the total cohort (N=20,089). Patients were censored at death or last engagement date.

Probability of All-Cause Mortality

- All-cause mortality patterns between the two categories of high-risk patients (age or prior event) were similar (**Figure 4**)

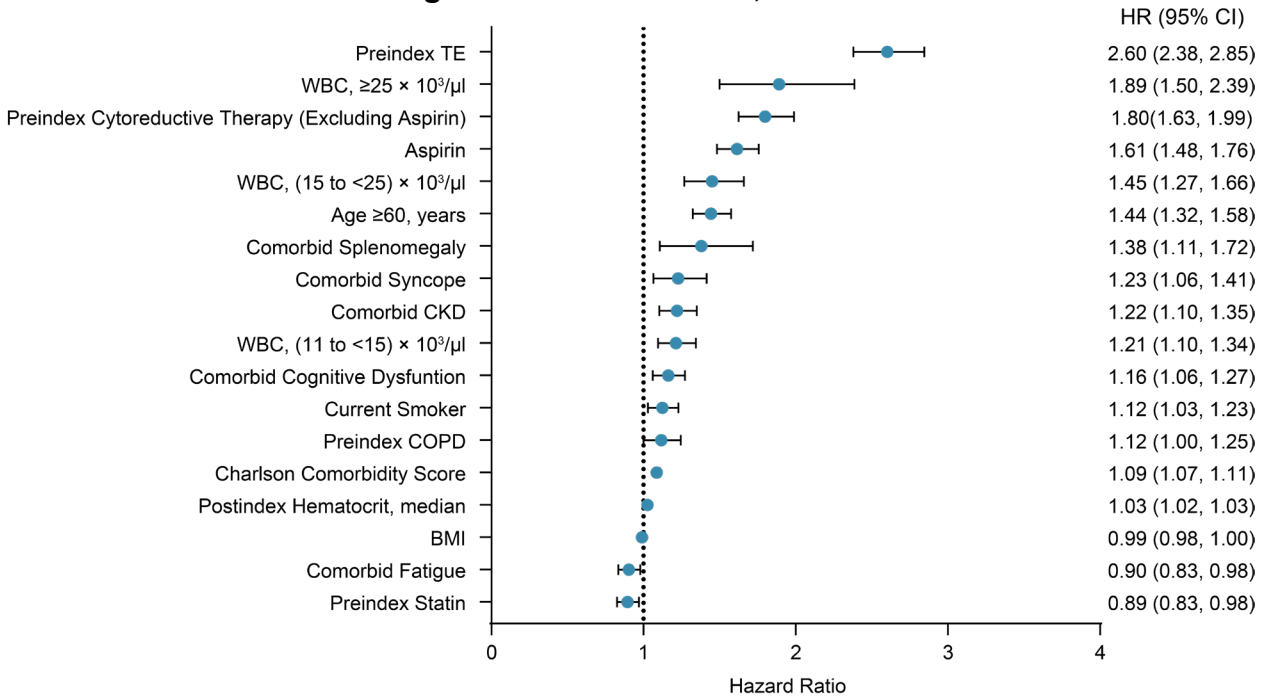
Figure 4. Kaplan-Meier Analysis Evaluating Probability of All-Cause Mortality



Cox Proportional Hazards Model, Time to TE

- The strongest predictor of post-index TE was prior TE (HR 2.6, 95% CI: 2.38-2.85)
- Each 1% increase in median post-index hematocrit was associated with a 3% increase in TE hazard (HR 1.026, 95% CI: 1.02-1.03)

Figure 5. Cox PH Model, Time to TE

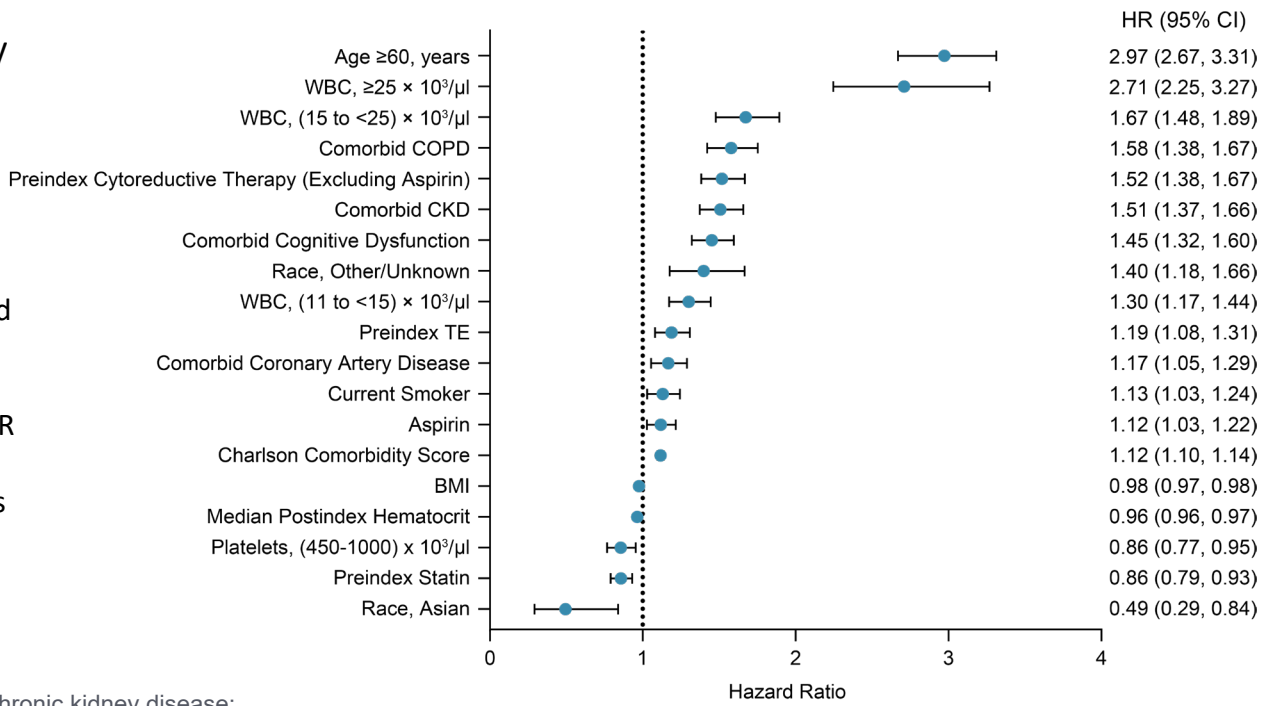


BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; PH, proportional hazards; PV, polycythemia vera; TE, thromboembolic event; WBC, white blood cell.

Cox Proportional Hazards Model, Time to Death

- Factors associated with higher hazard of mortality were largely similar but not identical to the predictors of TE:
  - Age ≥60 was the strongest predictor of mortality
  - Notably, prior TE, which was the strongest factor associated with the hazard of post-index TE, was not a particularly notable predictor of death, (HR 1.19, 95% CI: 1.08-1.31), compared with factors such as elevated WBC, and cardiovascular/respiratory comorbidities

Figure 6. Cox PH Model, Time to Death



BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; PH, proportional hazards; TE, thromboembolic event; WBC, white blood cell.

Conclusions

- Findings from this large, real-world analysis indicated that PV patients experience high rates of arterial and venous TE and death
- Event-based high-risk patients had a substantially higher probability of additional TE during the outcome period compared with age-based high-risk and low-risk patients
- While patients with a prior history of TE had the highest thromboembolic risk, all patients with PV were at high risk of TE, indicating that thrombotic risk reduction should remain a focus across all risk groups

PV, polycythemia vera; TE, thromboembolic event.

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Thank you