Thrombosis Before Diagnosis: A 22-Year National Analysis of Missed Opportunities in Polycythemia Vera and Essential Thrombocythemia

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Introduction

Polycythemia vera (PV) and essential thrombocythemia (ET) are BCR-ABL-negative myeloproliferative neoplasms (MPNs) associated with elevated arterial and venous thrombotic risk. Thrombosis often precedes diagnosis and may be the first manifestation of disease. However, whether MPNs are recognized or recorded as contributing factors in thrombotic deaths remains uncertain. Prior literature, including data from the European Collaboration on Low-Dose Aspirin in Polycythemia Vera (ECLAP) study and the European Leukemia Net (ELN) study (aka EXELS registry) has highlighted this diagnostic latency, but no US-based mortality study has quantified it on a population level.

Objectives

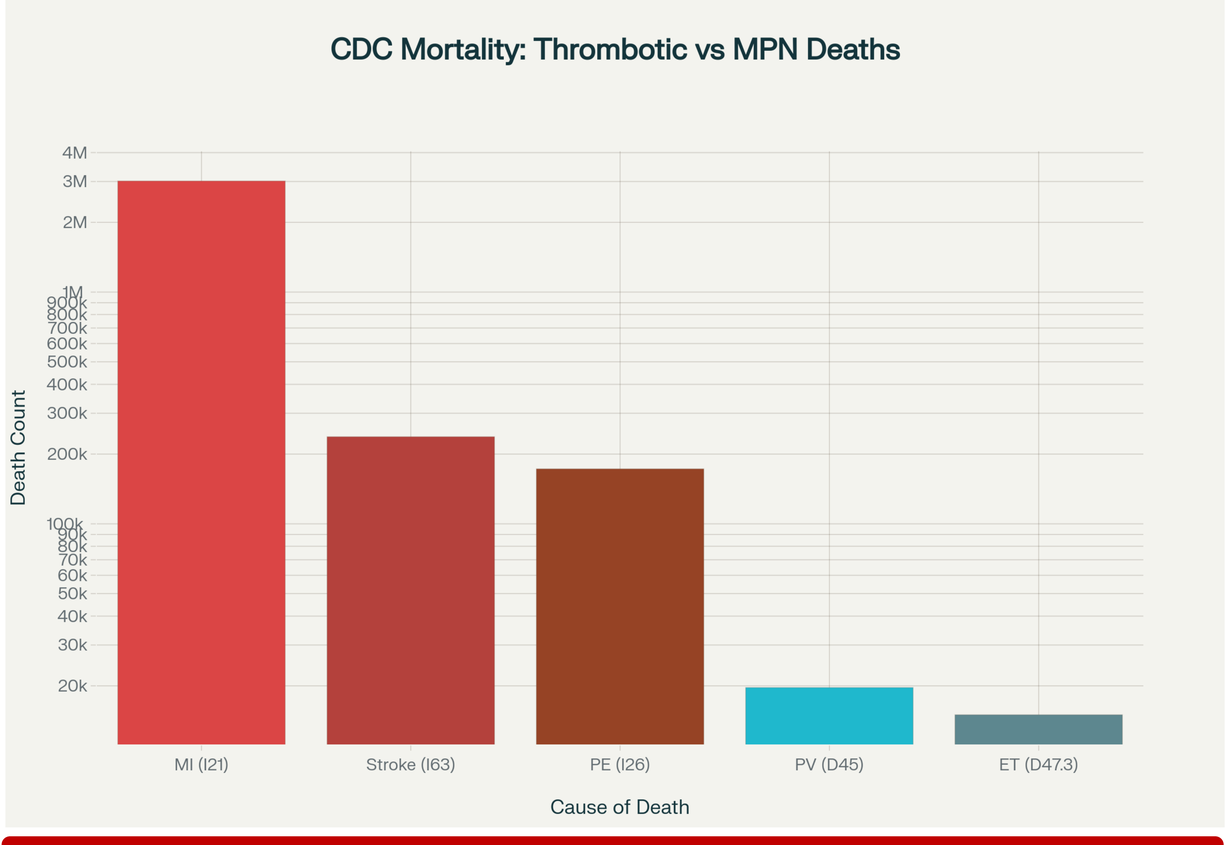
Assess temporal trends in thrombotic deaths and their attribution to PV or ET over a 22-year period in the US, with attention to under recognition on death certificates

Methods

We analyzed CDC WONDER mortality data (1999–2020) including ICD-10 codes for PV (D45), ET (D47.3), myocardial infarction (I21.x), pulmonary embolism (I26.x), and ischemic stroke (I63.x). Deaths were grouped by year and cause. We evaluated MPN death frequency, thrombotic mortality trends, and co-occurrence patterns.

Results

Across 22 years, thrombotic events accounted for over 3.4 million deaths, including myocardial infarction (>2.7 million), pulmonary embolism (~180,000), and ischemic stroke (~500,000). In contrast, only ~6900 deaths were attributed to PV or ET combined. MPN-related deaths remained stable (annual range: 290–329), while thrombotic deaths showed a mild decline after 2005. Critically, MPNs were rarely listed as underlying causes on certificates for patients who died of thrombotic complication, despite being biologically linked to hypercoagulability. No temporal increase in co-certification was observed over two decades.



Conclusion

This national study reveals a profound under-recognition of MPNs in thrombotic mortality reporting. The near-total absence of PV/ET attribution in patients dying of myocardial infarction, pulmonary embolism, or stroke suggests persistent diagnostic delays or failure to document contributing hematologic disease. Our findings underscore the need for earlier hematologic evaluation in patients with unexplained or atypical thrombosis, and call for systematic changes in death certification practices to better reflect MPN-associated mortality.