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Original Article

Retrospective Observational Study of Classical Philadelphia-Negative Myeloproliferative Neoplasms: Evaluating the Impact of the Triple-A Model on Thrombosis, Bleeding, Myelofibrosis, and Leukaemic Transformation in a Single Centre Over Ten Years.

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Abstract

Classical Philadelphia-negative myeloproliferative neoplasms (MPNs) are clonal disorders prone to thrombosis, bleeding, fibrosis, and leukaemic transformation. Prognostic models such as IPSET-Thrombosis, DIPSS, and MIPSS70 require molecular or cytogenetic data that are often inaccessible in low-resource settings. The Triple-A (Age, Absolute Neutrophil Count, Absolute Lymphocyte Count) model is a simple, cost-free alternative recently validated internationally, but its local performance is unknown.

Objectives: To evaluate relationships between Triple-A risk categories and major complications, and to assess survival across MPN subtypes in a Sri Lankan cohort.

A retrospective observational study (2014–2024) included 113 patients with ET (37.2 %), PV (38.9 %), and PMF (23.9 %). Baseline demographics, laboratory data, complications, and outcomes were extracted from unit registries. Kaplan–Meier and Cox regression analyses evaluated survival and predictors of mortality.

Median age 66 years (IQR 58.5–72); 54 % female. Arterial thrombosis 6.2 %, fibrotic transformation 3.5 %, overall mortality 8.8 %. Triple-A risk distribution: Low 9.7 %, Intermediate I 35.4 %, Intermediate II 23.0 %, High 31.9 %. Survival differed by diagnosis (Log-Rank $\chi^2 = 8.9$, $p = 0.012$) and risk category ($\chi^2 = 11.0$, $p = 0.012$). Independent predictors of mortality were Age ($p = 0.007$) and low ALC ($p = 0.013$).

The Triple-A model effectively stratifies MPN patients using routine parameters. Older age and lymphopenia predict poorer survival, supporting routine adoption of Triple-A risk assessment in Sri Lanka.

Keywords

Myeloproliferative neoplasms; Essential thrombocythaemia; Polycythaemia vera; Primary myelofibrosis; Triple-A model;

Introduction

Classical Philadelphia-negative myeloproliferative neoplasms—essential thrombocythaemia (ET), polycythaemia vera (PV), and primary myelofibrosis (PMF)—are chronic clonal stem-cell disorders originating from acquired driver mutations, most commonly JAK2 V617F, CALR, or MPL . The original Polycythaemia Vera Study Group (PVSG) criteria laid the foundation for diagnosis in the 1970s, later refined in the WHO 2016 and 2022 classifications integrating molecular data and marrow morphology.

While these advances improved diagnostic precision, they also increased dependence on expensive molecular testing. In low- and middle-income countries, including Sri Lanka, access to comprehensive molecular profiling is limited to tertiary centres. Consequently, clinicians must rely on accessible haematological and clinical parameters for prognostication and treatment decisions.

Traditional scoring systems—IPSET-Thrombosis for ET, PVSG/ELN for PV, and DIPSS/MIPSS for PMF—perform well but are disease-specific and variably applicable when mutation data are incomplete. To address this, Tefferi et al. [4] proposed the Triple-A

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model, which incorporates:

Age (>70 years = 4 points), Age (50-70 years=2points), Absolute Neutrophil Count (ANC) (≥ 8 × 10^9/L = 1 point) and Absolute Lymphocyte Count (ALC) (< 1.7 × 10^9/L = 1 point).

Scores classify patients into Low (0-1), Intermediate-I (2-3), Intermediate-II (4), and High (5-6) risk groups with distinct survival curves [4,5,6]. The model's simplicity, using data available from a complete blood count, makes it particularly attractive in resource-constrained environments.

However, regional validation is essential because demographic, genetic, and environmental factors may influence outcomes. This study therefore aimed to evaluate the impact of Triple-A risk stratification on thrombosis, bleeding, fibrotic or leukaemic transformation, and overall survival among patients managed at Teaching Hospital Jaffna over ten years.

Methods

A retrospective, single-centre observational study was conducted in the Haematology Unit, Teaching Hospital Jaffna—the main tertiary referral centre for Northern Sri Lanka. All consecutive patients diagnosed with ET, PV, or PMF from January 2014 to December 2024 were eligible. Cases of secondary erythrocytosis or thrombocytosis and Philadelphia-positive CML were excluded.

Diagnoses followed the 2016 WHO criteria, requiring characteristic blood counts, bone-marrow morphology, and exclusion of BCR: ABL1 rearrangement by RT-PCR. Molecular testing for JAK2 V617F was available in all patients; CALR and MPL mutations were done when clinically indicated.

Data were retrieved from the bone marrow biopsy registry, clinic databases, and paper records using a standard proforma. Variables included age, sex, baseline ANC and ALC, haemoglobin, haematocrit, platelet count, mutation status, therapy (hydroxyurea, phlebotomy, ruxolitinib, aspirin), and comorbidities (hypertension, diabetes, ischemic heart disease). Complications documented were: Arterial thrombosis: stroke, myocardial infarction, peripheral arterial event, Venous thrombosis: deep-vein thrombosis or pulmonary embolism, Haemorrhage: clinically significant bleeding requiring transfusion or hospitalization, and transformation: progression to myelofibrosis or acute leukaemia confirmed by marrow biopsy.

Follow-up was performed every 1-2 months in the clinic; survival status was confirmed from medical records or telephone review. The study cut-off date was 31 December 2024.

Analyses were performed with IBM SPSS v26. Continuous variables are presented as mean ± SD or median (IQR), categorical variables as frequencies and percentages. Comparisons used χ^2 or t-tests as appropriate. Overall survival (OS) was measured from diagnosis to death or last follow-up and estimated using Kaplan–Meier curves; differences were evaluated with the Log-Rank (Mantel-Cox) test. Cox proportional hazards regression identified independent predictors of mortality. Variables with $p < 0.10$ in univariate analysis were entered into multivariate models. Assumptions of proportional hazards were checked graphically by log-minus-log plots. A two-sided $p < 0.05$ was considered significant.

Ethics approval was granted by the Ethics Review Committee of Teaching Hospital Jaffna (Ref No: SO4/07/2025). All data were de-identified; no personal information was stored outside hospital servers.

Results

Patient Characteristics

A total of 113 patients met inclusion criteria (52 males, 61 females). The mean age was 63.9 ± 12.5 years (range 18–88), with median 66 years (IQR 58.5–72). PV was most common (38.9%), followed by ET (37.2 %) and PMF (23.9 %). Median follow-up was 56 months (range 12–120). Hypertension and diabetes were present in 43 % and 28 %, respectively. JAK2 V617F mutation was detected in 81 % of PV and 64 % of ET cases.

Complications and Outcomes

Arterial thrombosis occurred in 7 patients (6.2 %); 4 developed post-PV myelofibrosis (3.5 %). No documented venous thrombosis, major bleeding or acute leukaemic transformation occurred during the observation period. Overall mortality was 8.8 % (10 patients).

Triple-A Risk Distribution

Low risk: 9.7 %, Intermediate-I: 35.4 %, Intermediate-II: 23.0 %, High: 31.9 %. High-risk patients were older (median 71 years) and had lower ALC (mean 1.2 × 10^9/L) than others ($p < 0.01$).

Survival Analysis by Diagnosis

Overall survival differed significantly between diagnostic groups (Log-Rank $\chi^2 = 8.905$, $p = 0.012$). Pairwise comparisons showed inferior survival for PMF versus ET ($p = 0.021$) and PMF versus PV ($p = 0.026$). Median estimated survival: ET ≈ 102 months, PV ≈ 136 months, PMF ≈ 78 months.

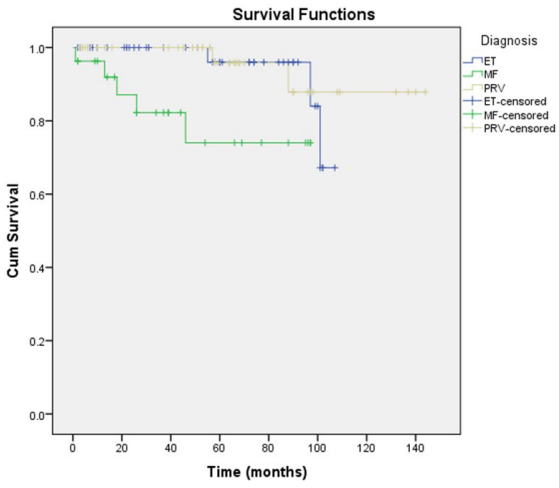

Figure 1. Kaplan–Meier overall survival curves by diagnosis (ET, PV, PMF).

Survival by Triple-A Risk

Significant differences were noted (Log-Rank $\chi^2 = 11.02$, $p = 0.012$). Low-risk patients had > 95 % 10-year survival, while high-risk cases fell below 50 % by 96 months. Intermediate-II showed an inflection after seven years.

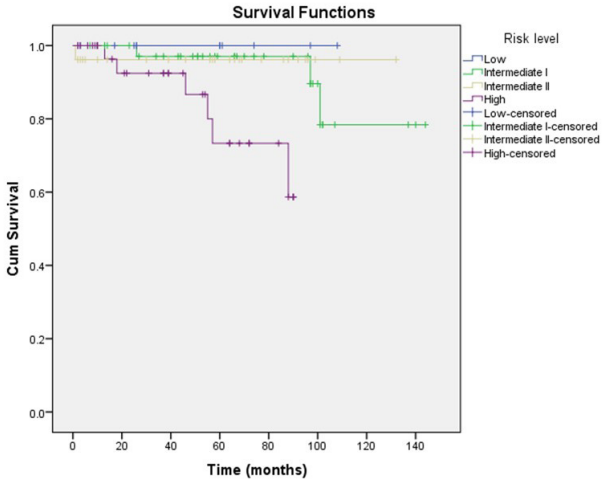

Figure 2. Kaplan–Meier survival curves by Triple-A risk category (Low, Int I, Int II, High).

Multivariate Cox model identified: Age ($\beta = 0.11$, $p = 0.007$, HR 1.12 [1.03–1.21]) and Low ALC ($\beta = 0.75$, $p = 0.013$, HR 2.11 [1.17–3.81]) as independent predictors of mortality. ANC, JAK2 status, and sex were not significant.

Discussion

This ten-year single-centre analysis demonstrates that the Triple-A model, based solely on age and differential counts, reliably stratifies prognosis in Sri Lankan MPN patients. The stepwise decline in survival across risk groups parallels international findings [4-6]. Our median survival of over 11 years for ET and PV is comparable to Western cohorts, supporting the general applicability of the model.

The strong predictive value of low ALC confirms emerging evidence that lymphopenia reflects immunological dysregulation and chronic inflammation in MPNs [7, 8]. Age, a well-recognized determinant of vascular and clonal events, remained the dominant predictor of mortality.

The low thrombosis rate (6.2 %) compared with European series (10–20 %) may relate to younger age at presentation, routine aspirin use, and lower incidence of metabolic syndrome in our population. Similarly, the absence of AML transformation may reflect shorter follow-up and effective cytoreductive control. Female predominance (54 %) and median age (66 years) mirror regional data from India and Southeast Asia, suggesting demographic consistency.

The Triple-A model offers a rapid, no-cost risk tool suitable for routine clinics and laboratory-based audits. Patients categorized as High risk require closer follow-up, aggressive management of cardiovascular risk factors, and consideration for cytoreductive therapy. Conversely, Low risk patients may be monitored with less frequent visits, optimizing resource use.

While IPSET and DIPSS integrate age and blood counts, they require distinct models for different MPNs and often depend on molecular markers. Triple-A provides a pan-MPN framework usable where genotyping is incomplete, making it particularly valuable for district hospitals. Importantly, its reproducibility across ethnic groups reinforces its universality.

Limitations were it was a Single-centre, retrospective design limits external validity, Sample size moderate; rare events such as venous thrombosis or leukaemic transformation may be under-represented and the treatment heterogeneity was not controlled in survival analysis.

Despite these, the study provides one of the first South Asian validations of the Triple-A model and adds to growing evidence that basic haematological indices retain powerful prognostic value.

Conclusions

The Triple-A model effectively stratifies Sri Lankan patients with MPNs by prognosis using routine blood parameters. Age and lymphopenia independently predict poorer survival. Adoption of this tool can support risk-adapted management and efficient follow-up scheduling in resource-limited settings.

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