Hypocellular Bone Marrow as an Independent Adverse Prognostic Feature in Primary Myelofibrosis:A Real-World Analysis of 241 Patients

Elmir Guluyev, MD[1,2] • Madad Abbasov, MD[1] • Gulnar Garayeva, MD[2] • Azer Kerimov, MD, PhD[2]

[1] Main Clinical Hospital of the Ministry of Defense of Azerbaijan, Baku, Azerbaijan [2] National Hematology and Transfusiology Center, Baku, Azerbaijan

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Background

- Primary myelofibrosis (PMF) encompasses a spectrum of myeloproliferative and myelodepletive/cytopenic phenotypes with distinct clinical and biological features.
- The myelodepletive phenotype is characterized by cytopenias, advanced marrow fibrosis, and inferior outcomes and is more frequently associated with hypocellular bone marrow [1–3].
- Although cytopenic PMF is recognized as a high-risk phenotype, the prognostic contribution of BM hypocellularity itself remains incompletely defined in contemporary PMF cohorts [4,5].

Aim

- Test whether hypocellular bone marrow identifies a distinct high-risk PMF subgroup beyond standard IPSS risk.
- Primary endpoint: overall survival by bone marrow cellularity.

Methods

- 241 consecutive PMF patients; BM cellularity available in 212 (hypercellular n=166, hypocellular n=45; 1 normocellular case excluded).
- Baseline comparisons: Mann–Whitney U and Fisher exact tests.
- OS from diagnosis to death/last follow-up; 71 deaths; median follow-up 43 months; Kaplan–Meier + log-rank.
- Multivariable logistic regression evaluated the association between BM hypocellularity and mortality after adjustment for clinical prognostic variables.

Conclusions

- Hypocellular BM identifies a distinct myelodepletive PMF phenotype characterized by severe cytopenias, advanced fibrosis, higher mortality, and markedly shorter survival.
- The persistence of excess mortality within the same IPSS categories suggests that BM cellularity may provide prognostic information beyond conventional clinical risk stratification.
- These findings warrant validation in larger, molecularly characterized cohorts and evaluation of BM cellularity as a potential adjunct to existing PMF prognostic models.

51.1% vs 21.1%
Mortality
P < 0.001

57.2 mo vs NR
Median overall survival
Log-rank P < 0.001

9.3 vs 12.0 g/dL
Hemoglobin
P < 0.001

80% vs 18.4%
Mortality in IPSS low-risk
Hypocellular vs hypercellular

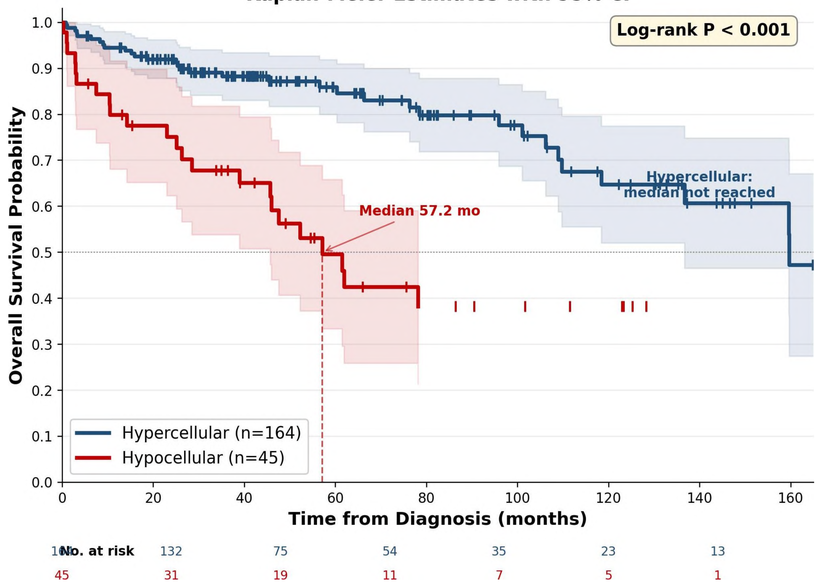
Results

Baseline characteristics by bone marrow cellularity

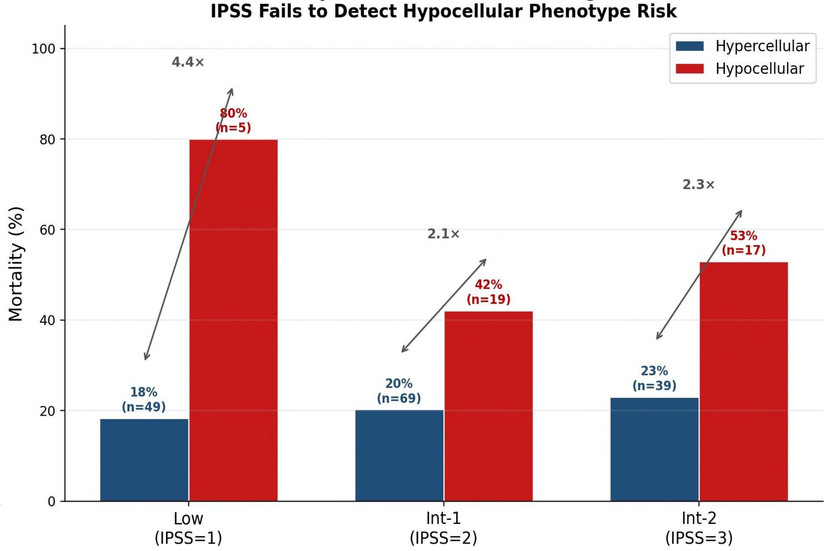
Characteristic	Hypercellular (n=166)	Hypocellular (n=45)	P value
Mortality, %	21.1	51.1	< 0.001
Median OS, months	Not reached	57.2	< 0.001
Hemoglobin, g/dL	12.0	9.3	< 0.001
Hemoglobin < 10 g/dL, %	28.7	64.4	< 0.001
WBC, ×10⁹/L	13.8	9.2	0.002
Platelets, ×10⁹/L	438.0	199.5	< 0.001
LDH, U/L	489	584	0.037
Spleen size, cm	18.7	22.1	< 0.001
High-grade fibrosis (MF ≥ 2), %	71.6	95.3	0.001
Neutrophil-to-lymphocyte ratio	4.4	2.5	0.002

Lower NLR in hypocellular PMF (2.5 vs 4.4) is consistent with marrow failure rather than inflammatory activation — a plausible reason standard IPSS may underestimate risk in this phenotype.

Overall Survival by Bone Marrow Cellularity in PMF
Kaplan-Meier Estimates with 95% CI



Mortality Within Identical IPSS Categories
IPSS Fails to Detect Hypocellular Phenotype Risk



Across identical IPSS strata, hypocellular patients had consistently higher mortality, indicating prognostic information not captured by IPSS alone.

Abbreviations

BM, bone marrow; IPSS, International Prognostic Scoring System; OS, overall survival; PMF, primary myelofibrosis; NLR, neutrophil-to-lymphocyte ratio; LDH, lactate dehydrogenase; NR, not reached.

Contact

Madad Abbasov, MD
Department of Hematology, Main Clinical Hospital of the Ministry of Defense of Azerbaijan, Baku
mededabbasov@gmail.com • ORCID: 0009-0005-7748-0545

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