How to Use Prognostic Risk Scoring and Symptom Burden Assessment to Tailor Myelofibrosis Treatment

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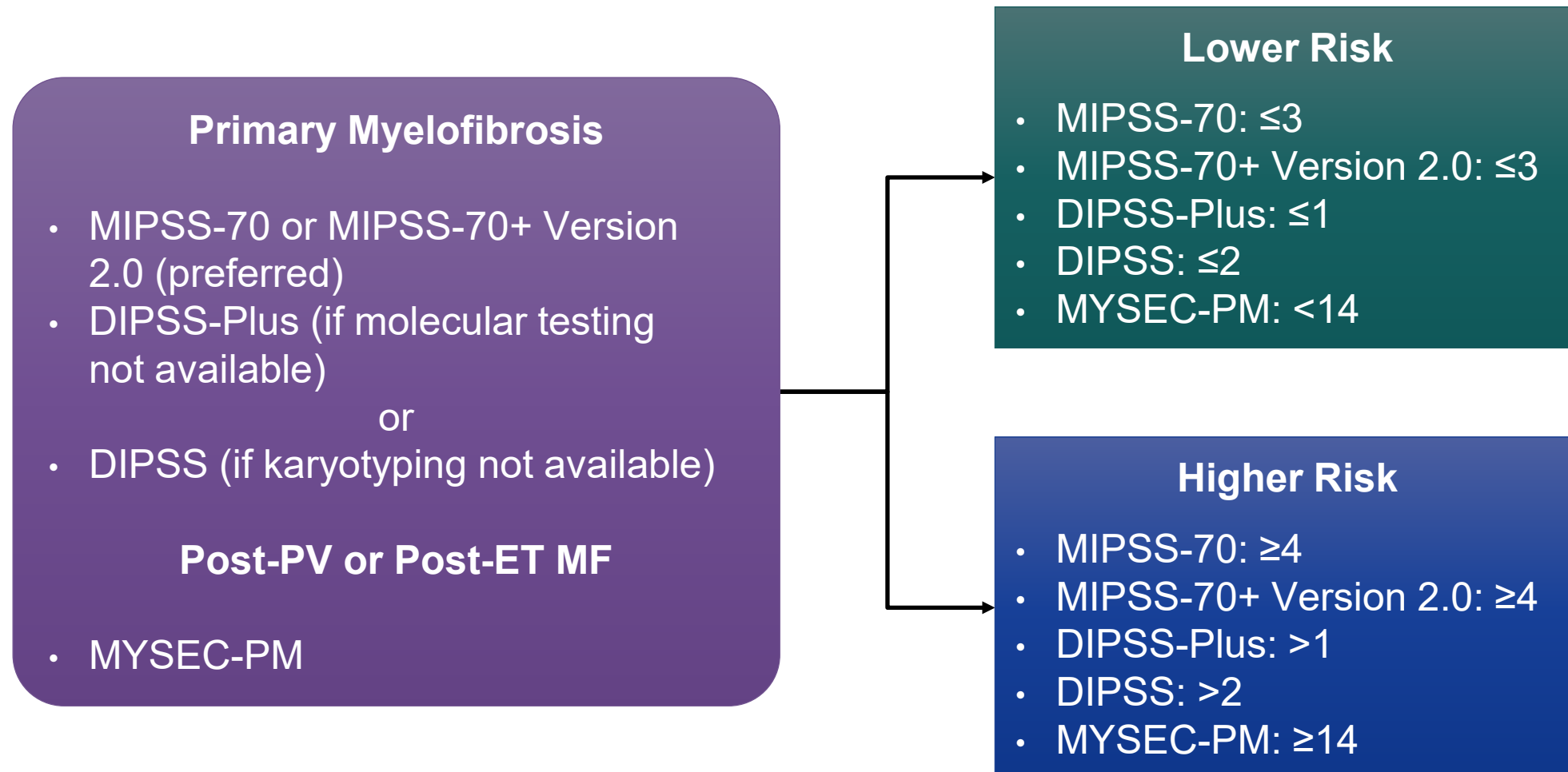Assistant in Medicine
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Risk Stratification Has Become a Critical Aspect of Planning for Appropriate Therapy[1]

Risk Stratification

Primary Myelofibrosis

- MIPSS-70 or MIPSS-70+ Version 2.0 (preferred)
- DIPSS-Plus (if molecular testing not available)

or

- DIPSS (if karyotyping not available)

Post-PV or Post-ET MF

- MYSEC-PM

Lower Risk

- MIPSS-70: ≤3
- MIPSS-70+ Version 2.0: ≤3
- DIPSS-Plus: ≤1
- DIPSS: ≤2
- MYSEC-PM: <14

Higher Risk

- MIPSS-70: ≥4
- MIPSS-70+ Version 2.0: ≥4
- DIPSS-Plus: >1
- DIPSS: >2
- MYSEC-PM: ≥14

1. Gerds AT, et al. NCCN Guidelines. Myeloproliferative Neoplasms (Version 1.2024). NCCN.org.

Prognostic Models of Myelofibrosis[1]

Parameter	IPSS[2]	DIPSS[3]	DIPSS-Plus[4]	MIPSS70[5,6,d]	MYSEC-PM[7]
Age > 65 yr	Yes (1 pt)	Yes (1 pt)	Yes[a]		
Age (0.15 pt/yr) at diagnosis of secondary MF					Age (yr)
Hgb < 10 g/dL	Yes (1 pt)	Yes (2 pts)	Yes[a]	Yes (1 pt)	
Hgb < 11 g/dL					Yes (2 pts)
WBC > 25 x 10^9/L	Yes (1 pt)	Yes (1 pt)	Yes[a]	Yes (2 pts)	
PB blood blasts ≥ 1%	Yes (1 pt)	Yes (1 pt)	Yes[a]		
PB blood blasts ≥ 2%				Yes (1 pt)	
Circulating blasts ≥ 3%					Yes (2 pts)
Constitutional symptoms	Yes (1 pt)	Yes (1 pt)	Yes[a]	Yes (1 pt)	Yes (1 pt)
Unfavorable karyotype[b]	No	No	Yes (1 pt)		
RBC transfusion dependence[c]	No	No	Yes (1 pt)		
Platelet < 100 x 10^9/L	No	No	Yes (1 pt)	Yes (2 pts)	
Platelet < 150 x 10^9/L					Yes (1 pt)
Grade ≥ 2 BM fibrosis				Yes (1 pt)	
Absence of *CALR* Type 1				Yes (1 pt)	
CALR-unmutated genotype					Yes (2 pts)
HMR category*				Yes (1 pt)	
≥2 HMR mutations				Yes (2 pts)	
Can be used at any time	No (only at diagnosis)	Yes	Yes		

[a] Zero, 1, 2, and 3 points are assigned to DIPSS categories of low, intermediate-1, intermediate-2, and high risk, respectively; features are not weighted individually.
[b] Complex karyotype or a single or 2 abnormalities including +8, -7/7q-, i(17q), -5/5q-, 12p-, inv(3), or 11q23 rearrangement. [c] Presentation with symptomatic anemia necessitating RBC transfusion at time of referral, or a history of RBC transfusions for myelofibrosis-associated anemia, without regard to the number of RBC transfusions. [d] Age <70 years.
* HMR category = any mutations in *ASXL1*, *EZH2*, *SRSF2*, *IDH1/2*.
DIPSS, Dynamic International Prognostic Scoring System; Hgb, hemoglobin; IPSS, International Prognostic Scoring System; MIPSS70, Mutation-Enhanced International Prognostic Scoring System age ≤70 years; MYSEC-PM, Myelofibrosis Secondary to PV and ET Prognostic Model; PB, peripheral blood; RBC, red blood cell; WBC, white blood cell count.

1. Bose P, Verstovsek S. *Cancer*. 2016;122(5):681-692. 2. Cervantes F, et al. *Blood*. 2009;113(13):2895-2901. 3. Passamonti F, et al. *Blood*. 2010;115(9):1703-1708. 4. Gangat N, et al. *J Clin Oncol*. 2011;29(4):392-397. 5. Guglielmelli P, et al. *J Clin Oncol*. 2018;36(4):310-318. 6. Tefferi A, et al. *J Clin Oncol*. 2018 36(17):1769-1770. 7. Passamonti F, et al. *Leukemia*. 2017;31(12):2726-2731.

Survival Varies by Risk[1]

Median Survival, Years					
Risk Group	IPSS[2]	DIPSS[3]	DIPSS-Plus[4]	MIPSS70[5]	MYSEC-PM[6]
Low	11.3	Not reached	15.4	27.7	NR
Intermediate-1	7.9	14.2	6.5	7.1*	9.3
Intermediate-2	4.0	4.0	2.9		4.4
High	2.3	1.5	1.3	2.3	2

Gaps in Myelofibrosis Risk Assessments Impact Treatment Initiation

- Real-world assessment of physician-assigned risk categorization and treatment initiation
  - 491 patients with MF from 45 US-based community hematology/oncology practices
    - Physician-assigned vs data-derived IPSS risk categorization at diagnosis
    - 69% primary MF
    - Risk categorization was not assigned in 30% of patients; scoring system was used in 50% of patients who were scored
      - 43% of physician-assigned risk categorizations were incorrect compared to data-derived scoring; 85% underestimations
    - Patients with underestimated risk were significantly less likely to receive any treatment (pharmacologic or HCT referral)

Verstovsek S, et al. *Ann Hematol*. 2020;99(11):2555-2564.

Symptom Burden in MF: Wide Range of Constitutional Symptoms

Fever

Fatigue

Bone pain

Depression & anxiety

Night sweats

Constellation of MF signs and symptoms

Early satiety

Sexual dysfunction

Weight loss

Pruritus

Concentration issues

Yoon J, Pettit K. *Expert Rev Hematol*. 2021;14(7):607-619. Verstovsek S, et al. *Leukemia*. 2016;30(6):1413-1415. Cervantes F, et al. *Expert Rev Hematol*. 2016;9(5):489-496.
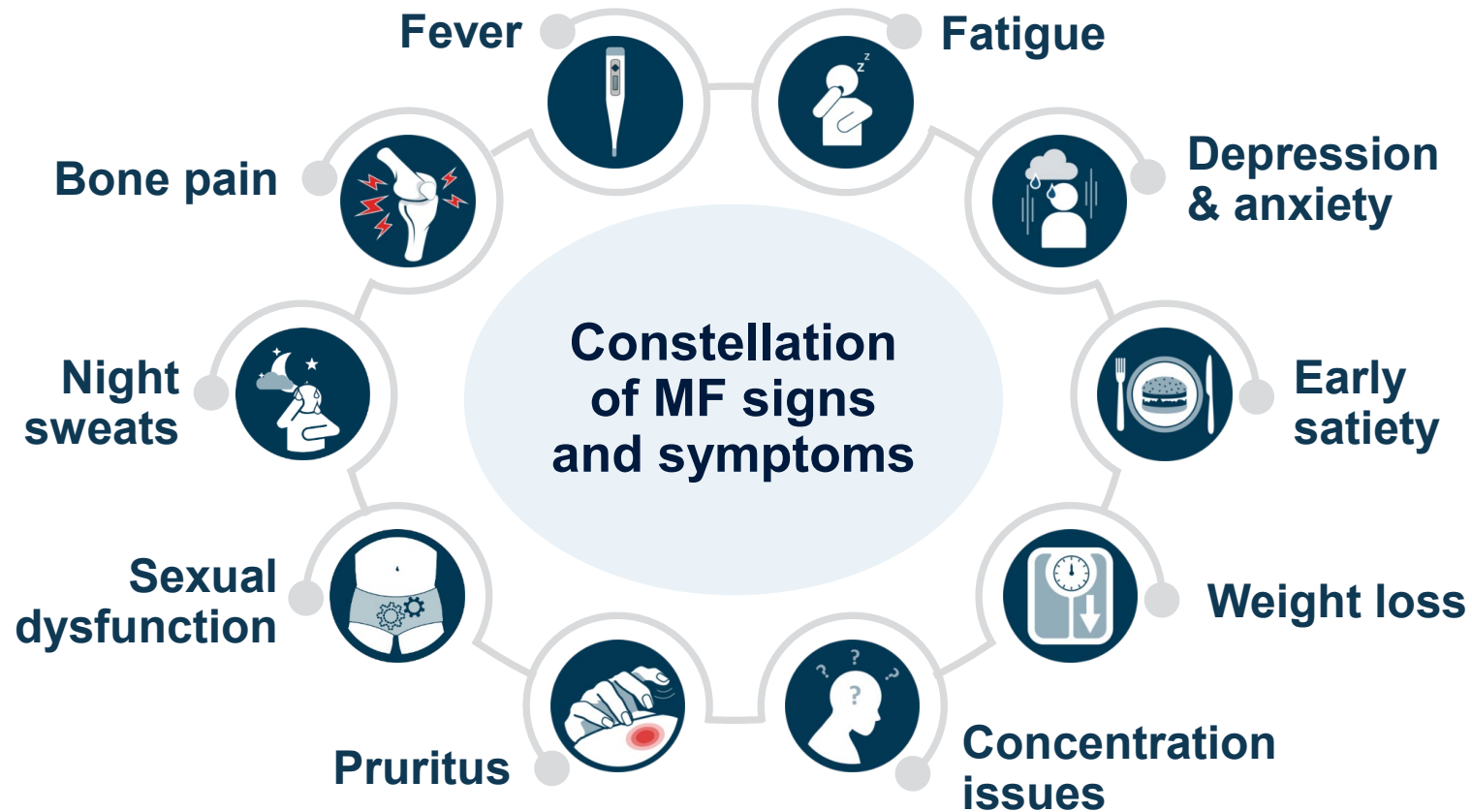
Assessing Symptoms in MF: MPN-SAF TSS (MPN-10)

- **Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS)**
  - 10-symptom assessment scale for MPNs
  - Each symptom is rated on a 0 to 10 scale from absent (0) to worst imaginable (10)
  - Total possible score: 100

| Symptom	1 to 10 (0 if absent) ranking 1 is most favorable and 10 least favorable
Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your WORST level of fatigue during past 24 hours	(No Fatigue) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)

Circle the one number that describes, during the past week, how much difficulty you have had with each of the following symptoms

Filling up quickly when you eat (early satiety)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Abdominal discomfort	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Inactivity	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Problems with concentration- compared to prior to my MPD	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Night sweats	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Itching (pruritus)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Bone pain (diffuse not joint pain or arthritis)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Fever (>100 F)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Daily)
Unintentional weight loss last 6 months	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)

Emanuel RM, et al. *J Clin Oncol*. 2012;30(33):4098-4103.

Symptom Burden Profile in MF With Thrombocytopenia

Significant:

- Brief Fatigue Index
- Worst fatigue
- Early satiety
- Inactivity
- Dizziness
- Sad mood
- Cough
- Night sweats
- Itching
- Fever
- Weight loss
- Overall QoL

QOL, quality of life.
Scotch AH, et al. *Leuk Res*. 2017;63:34-40.
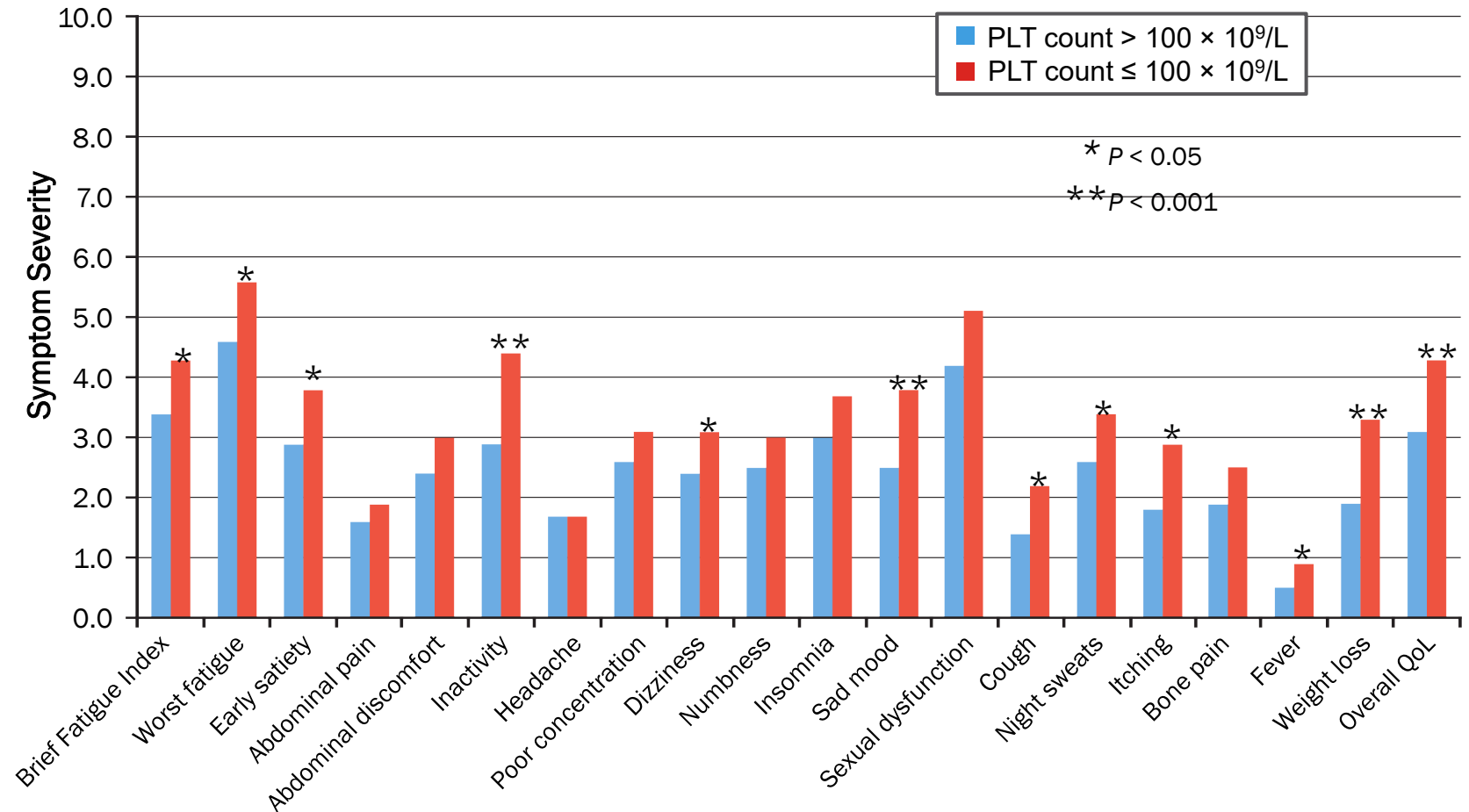
Summary

- Risk stratification is a key first step when evaluating a patient with myelofibrosis

- Risk groups predict survival and inform therapy decisions
  - Real-world data suggest risk assessments are underutilized

- Patients with cytopenia have a significant symptom burden