Myelodysplastic Syndromes and Acute Myeloid Leukemia in the Elderly

Heidi D. Klepin, MD, MS

KEYWORDS

• Myelodysplasia • Acute myeloid leukemia • Older • Treatment • Management • Elderly

KEY POINTS

- Myelodysplastic syndromes (MDS) are a heterogeneous group of hematologic disorders with variable natural history.
- Treatment recommendations for MDS are risk adapted and range from supportive care to high-intensity therapy.
- Optimal therapy for older patients with acute myeloid leukemia (AML) is unclear.
- Management of older adults with MDS and AML needs to be individualized, accounting for both the heterogeneity of disease biology and patient characteristics, which can influence life expectancy and treatment tolerance.

MYELODYSPLASTIC SYNDROMES

Myelodysplastic syndromes (MDS) constitute a heterogenous group of clonal hematopoietic disorders characterized by ineffective hematopoiesis and peripheral blood cytopenias. MDS can be indolent or rapidly progressive with complications secondary to profound cytopenias and the risk of evolution into acute myeloid leukemia (AML). MDS also impair quality of life, and are associated with high symptom burden[1] and high rates of health care use. Estimated 3-year survival rates are less than 50% in aggregate,[2] although survival can vary widely based on risk stratification. MDS are most commonly diagnosed among older adults (80% among adults $\geq$70 years of age) with approximately 15,000 to 20,000 new cases per year in the United States.[3]

Disclosure: Dr H.D. Klepin is supported by a Paul Beeson Career Development Award in Aging Research (K23AG038361; supported by NIA, AFAR, The John A. Hartford Foundation, and The Atlantic Philanthropies), The Gabrielle's Angel Foundation for Cancer Research, and NCI Cancer Center Support Grant (CCSG) P30CA012197. Dr H.D. Klepin has no other disclosures.
Section on Hematology and Oncology, Department of Internal Medicine, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, USA
E-mail address: hklepin@wakehealth.edu

Clin Geriatr Med 32 (2016) 155–173
http://dx.doi.org/10.1016/j.cger.2015.08.010 **geriatric.theclinics.com**
0749-0690/16/$ – see front matter

Given population aging, these are diseases that will frequently be encountered in geriatric practices.

Diagnosis and Work-up

Diagnosis of MDS relies mainly on peripheral blood and bone marrow findings. The diagnosis should be suspected in individuals presenting with cytopenia. A common presentation is progressive macrocytic anemia followed by pancytopenia in older adults. Classic peripheral blood findings associated with MDS include macrocytosis and hypogranular, hypolobated (dysplastic) neutrophils. A bone marrow biopsy with cytogenetic analysis is required to confirm the diagnosis. Cytogenetic abnormalities (often involving chromosomes 5, 7, 8, 17, or 20) play a critical role in the diagnosis and natural history of MDS.

Risk Stratification: Disease Characteristics

Because of the heterogeneity inherent in diseases classified as MDS, several risk stratification schemes have been proposed to inform trial design and treatment decisions. The International Prognostic Scoring System (IPSS) is the most commonly referenced risk stratification schema and was developed to assess risk at the time of diagnosis.[4] The IPSS incorporates specific cytogenetic abnormalities, the percentage of marrow blasts, and the number of hematopoietic lineages involved in the cytopenia. A 5-category revised IPSS (IPSS-R) was developed, which further subdivides cytogenetic abnormalities and increases the weight of higher blast percentages.[5,6] The IPSS-R highlights differences in the natural history of the disease by contrasting survival and time to AML progression (**Table 1**). In the development cohort, age was a prognostic factor for survival but not for progression to AML, having more impact in lower versus higher risk disease. The IPSS does not account for severity of cytopenia or for transfusion dependence.

Risk Stratification: Patient Characteristics

Selection of treatment of patients with MDS depends not only on disease characteristics but on assessment of the patient's overall fitness and competing comorbid conditions. Patient characteristics that influence life expectancy and treatment tolerance (eg, comorbidity, functional status, cognition) vary widely among similarly aged patients. Although measurement of these characteristics is not routine in most clinical trials, there is evidence regarding the prevalence and prognostic importance of comorbidity.[7–9] Studies suggest that more than half of older adults diagnosed with MDS have competing comorbid conditions and that comorbidity is associated with

Table 1
Overall survival (OS) and risk of AML evolution by revised IPSS score

Risk Group	IPSS-R Score	Median OS (y)	Median Time to 25% AML Evolution (y)
Very low	<1.5	8.8	>14.5
Low	<1.5–3.0	5.3	10.8
Intermediate	>3–4.5	3.0	3.2
High	>4.5–6	1.6	1.4
Very high	>6	0.8	0.7

Abbreviation: IPSS-R, Revised International Prognostic Scoring System.

Data from Greenberg PL, Tuechler H, Schanz J, et al. Revised International Prognostic Scoring System (IPSS-R) for myelodysplastic syndromes. Blood 2012;120(12):2454–65.