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To the editor:

Can the revised IPSS predict response to erythropoietic-stimulating agents in patients with classical IPSS low or intermediate-1 MDS?

The "classical" International Prognostic Scoring System (IPSS), based on cytogenetics, marrow blast percentage, and number of cytopenias, has played a major role in prognosis assessment in myelodysplastic syndromes (MDS).[1] The recently published revised IPSS (IPSS-R), using the same parameters, but with 5 rather than 3 cytogenetic subgroups and new cutoff values for cytopenias and marrow blast percentages, refines the original IPSS prognostic value.[2,3] However, its prognostic value for response to erythropoiesis-stimulating agents (ESA) has not been assessed. We analyzed it retrospectively in 456 IPSS low/intermediate (Int)-1–risk MDS patients treated with ESA in France, Germany, and Italy.

Those 456 patients had serum erythropoietin (EPO) <500 mU/mL and hemoglobin (Hb) ≤10 g/dL and had received ESA (EPO alfa or β 40 000-60 000 IU/week, or darbepoetin 150-300 μg/week) for at least 12 weeks. In addition to IPSS-R parameters, age, sex, serum EPO level, serum ferritin (SF), red blood cell (RBC) transfusion requirement before ESA onset were assessed for response to ESA (based on International Working Group 2006 criteria), and overall survival (OS) from ESA onset. Characteristics of the 456 patients at ESA onset are listed in Table 1. Seventy-one percent of the patients had never received RBC transfusions, and their median Hb level was 9.3g/dL (range 7.0-10); 29% of patients had received at least 4 RBC concentrates/8 weeks before ESA onset (with a maximum of 12 concentrates). Median SF was 357 ng/mL and serum EPO was 60 mU/mL (range 6-483). IPSS was low in 55% and Int-1 in 45% of patients. IPSS-R was very low in 15%, low in 61%, intermediate in 19%, and high in 4% of the patients.

A total of 303 (61%) patients had an erythroid response, including 72% and 52% of low and Int-1 risk patients, respectively ($P = .001$). Using IPSS-R, 85%, 68%, 48%, and 31% of patients had erythroid response in the very low, low, intermediate, and high-risk groups, respectively ($P < .0001$).

Other prognostic factors of erythroid response, in univariate analysis, included individual IPSS-R parameters analyzed according to IPSS-R thresholds (Hb level, platelet count, absolute neutrophil count, marrow blast %, cytogenetics), serum EPO level, SF (variables tested as continuous variables), and previous RBC transfusions. In multivariate analysis, IPSS-R, serum EPO, and SF remained significantly associated with erythroid response ($P < .0001$, $P < .0001$, and $P = .002$, respectively).

Applying 1 point to each of the following unfavorable variables of response to ESA, serum EPO >200 mU/mL (=1), SF >350 ng/mL (=1), and IPSS-R (very low = 0, low = 1, intermediate = 2, and high = 3) yielded a score ranging from 0 to 4, with response rates of 85%, 80%, 64%, 40%, and 20%, respectively. As expected, IPSS-R also had strong prognostic value for OS (not shown).

Thus, in this patient cohort with overall favorable prognostic factors of response to ESA according to the Nordic score[4] (ie, serum EPO <500 mU/mL and no or limited transfusion dependence), IPSS-R alone, and even better, a score ≥3 (using IPSS-R, serum EPO, and SF) proved useful to identifying patients with low response to ESA who also have worse OS[5] and may require alternative treatments.

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Table 1. Baseline patient characteristics

	n = 456	Patients, %	Erythroid response (IWG 2006 criteria)	Univariate analysis *P*	Multivariate analysis *P*
Hb, g/dL					
<8	52	11	33		
8-10	292	64	66		
=10	112	25	78	<.0001	
ANC					
<0.8	42	9	55		
≥0.8	414	91	66	.16	
Platelet count*					
<50	17	3	37		
50-100	58	13	57		
>100	381	84	67	.01	
Marrow blasts, %					
≤2	238	52	72		
<2-<5	118	26	61		
5-10	100	22	53	.0052	
IPSS-R karyotype					
Very good	21	5	71		
Good	379	83	65		
Intermediate	45	10	75		
Poor-very poor	11	2	20	.008	
IPSS					
Low	256	55	72		
Int-1	210	45	52	.001	
IPSS-R					
Very low	69	15	85		
Low	281	61	68		
Intermediate	87	19	48		
High	19	4	31	<.0001	<.0001
Sex					
Male	250	55	62		
Female	206	45	68	.14	
Age, years					
≤60	29	6	55		
>60	427	94	66	.23	
EPO, mU/mL					
≤100	306	67	75		
>100	150	33	45	<.0002	
≤200	393	86	75		
>200	63	13	31	<.0001	<.0001
Serum ferritin, ng/mL					
≤350	224	49	72		
>350	232	51	58	.001	.002
Previous RBC transfusions					
No	323	71	73		
Yes	133	29	55	.0005	
WHO classification					
RA	110	24	73		
RAEB-1	69	15	50		
RARS	114	25	70		
RARS-T	2	0.3	100		
RCMD	124	27	62		
MDS WITH DEL 5q	21	5	62		
MDS-U	16	4	55	.03	.71

ANC, absolute neutrophil count; IWG, International Working Group; MDS-U, MDS-unclassified; MDS WITH DEL, MDS associated with isolated del (5q); RA, refractory anemia; RAEB-1, refractory anemia with excess blasts-1; RARS, refractory anemia with ring sideroblasts; RARS-T, refractory anemia with ring sideroblasts associated with marked thrombocytosis; RCMD, refractory cytopenia with multilineage dysplasia; WHO, World Health Organization.

Univariate and multivariate analyses for response (IWG 2006 criteria). The variables with significant prognostic value in univariate analysis were integrated in the multivariate analysis, excepting Hb, platelet count, IPSS-R karyotype, and % of blasts, because IPSS-R integrates already those variables. For EPO level, the 200 mUI/mL threshold was chosen because it was the most significant in univariate analysis. Previous transfusions were not integrated in the model because they "duplicate" the Hb variable.

*10^9/L.

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To the editor:

Impact of lead intoxication in children with iron deficiency anemia in low- and middle-income countries

Recently, Pasricha et al[1] reported on the control of iron deficiency anemia in low- and middle-income countries.

The article discusses common contributory etiologies ranging from nutritional to infectious causes for iron deficiency anemia in the pediatric age group. Given that lead ingestion exacerbates iron deficiency,[2-4] may accelerate the cognitive injuries of iron deficiency,[5] and may also confound the diagnosis of microcytic anemia, we were surprised that the authors did not mention lead in their article.

Clune et al[6] found that lead intoxication is remarkably common in many areas in the world including those described by the authors. Our own pilot study, conducted in a semiurban Indian setup, indicated strikingly high prevalence rates of lead intoxication. Fifty-six percent of the children in the age group of 0 to 6 years had a mean blood lead level (BLL) above 5 mcg/dL, with close to 10% of children in this age group having BLL dangerously above 15 mcg/dL.

Similar results were reported[7,8] in separate moderate to large population-based studies from different parts of India with an average BLL in toxic ranges, well above the upper limit set by the World Health Organization and the Centers for Disease Control and Prevention for acceptable BLLs.[9]

Increased existence of hotspots of lead exposure in the South Asian region exist, but the lack of universal lead-screening programs in the developing world underrecognizes lead poisoning as a significant health hazard. Given the geographical overlap, it is likely that many of the patients in the study of Pasricha et al had concomitant lead poisoning.

Given the value of the authors' discussion in creating awareness and perhaps initiating legislation on the global level, we think the likely contribution of lead intoxication should be brought to the attention of investigators and public health officials.

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