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ORIGINAL ARTICLE

Prognostic Impact of Transfusion Dependency in Patients with Lower-Risk Myelodysplastic Syndrome

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SUMMARY

Background: **This study retrospectively analyzed the prognostic impact of transfusion burden in patients with lower-risk myelodysplastic syndrome (LR-MDS) and the outcomes of each treatment option.**
Methods: **Data on 168 patients with LR-MDS between July 2011 and April 2020 were retrospectively reviewed. Non-transfusion dependent (NTD) was defined as no transfusion history in a period of 16 weeks, low transfusion burden (LTB) as receiving 3 - 7 red blood cell (RBC) units in a period of 16 weeks, and high transfusion burden (HTB) as receiving ≥ 8 RBC units in a period of 16 weeks.**
Results: **The treatment response was observed over 4 - 6 months after treatment. Among the 168 patients, 105 were treated with anabolic steroids (n = 65), erythroid stimulating agents (n = 12), or hypomethylating agents (n = 28). The overall response rate was 53.3% (56/105), with 53 patients showing hematologic improvement (50.5%). The clinical benefit rate was 78.1% (82/105). The 5-year overall survival (OS) rates were 75.5%, 45.8%, and 33.3% for NTD, LTB, and HTB, respectively (p = 0.001). The 5-year incidences of acute myeloid leukemia were 0%, 9.9%, and 32.5% in NTD, LTB, and HTB, respectively (p < 0.001). In the multivariate analysis, age (hazard ratio [HR] 1.04, p = 0.009), LTB (HR 3.77, p = 0.002), HTB (HR 4.59, p < 0.001), and hemoglobin response (HR 0.45, p = 0.036) were significant factors for OS.**
Conclusions: **Our findings show transfusion dependency is an adverse prognostic factor in LR-MDS. HTB presented a higher risk of leukemic transformation.**
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Supplementary Data

Table S1. Patient characteristics according to the treatment modalities (n = 168).

Variables	None	Steroid	ESA	HMA	p-value
Number of patients	63	64	12	29	
Age, median year (range)	62 (20 - 92)	65 (24 - 86)	69 (52 - 86)	64 (25 - 80)	0.338
Gender					
Male	32 (50.8)	35 (54.7)	7 (58.3)	20 (69.0)	0.433
Female	31 (49.2)	29 (45.3)	5 (41.5)	9 (31.0)	
WHO classification					
SLD	10 (15.9)	8 (12.5)	3 (25.0)	8 (27.6)	0.323
MLD	47 (74.6)	46 (71.9)	7 (58.3)	16 (55.2)	
RS-SLD	4 (6.3)	3 (4.7)	1 (8.3)	0	
RS-MLD	0	3 (4.7)	1 (8.3)	2 (6.9)	
EB-1	1 (1.6)	2 (3.1)	0	3 (10.3)	
del(5q)	1 (1.6)	2 (3.1)	0	0	
BM blast% *	1.0 (0 - 9.5)	1.2 (0 - 7.1)	0.8 (0.2 - 3.3)	1.4 (0 - 7.0)	0.501
Hb (g/dL) *	9.6 (5.3 - 14.7)	8.9 (4.3 - 14.7)	8.6 (6.3 - 11.1)	8.0 (4.9 - 13.5)	0.042
ANC ($\times 10^3$/L) *	1.41 (0.15 - 5.49)	1.23 (0.30 - 4.68)	1.41 (1.06 - 4.00)	1.22 (0.47 - 10.06)	0.695
Platelet ($\times 10^9$/L) *	95 (12 - 604)	63 (4 - 484)	71 (13 - 362)	68 (4 - 485)	0.716
Cytogenetic risk by IPSS-R					
Very good	3 (4.8)	5 (7.8)	1 (8.3)	3 (10.3)	0.850
Good	57 (90.6)	56 (87.5)	10 (83.3)	23 (79.3)	
Intermediate	3 (4.8)	3 (4.7)	1 (8.3)	3 (10.3)	
Erythropoietin level (n = 78)					
< 200 U/L	20 (76.9)	17 (58.6)	5 (62.5)	7 (46.7)	0.511
200 - 500 U/L	3 (11.5)	5 (17.2)	1 (12.5)	2 (13.3)	
> 500 U/L	3 (11.5)	7 (24.1)	2 (25.0)	6 (40.0)	
Transfusion burden					
Non-transfusion dependent	57 (90.5)	39 (60.9)	7 (58.3)	10 (34.5)	< 0.001
Low transfusion burden	5 (7.9)	20 (31.3)	5 (41.7)	4 (13.8)	
High transfusion burden	1 (1.6)	5 (7.8)	0	15 (51.7)	
IPSS-R risk group					
Very low	17 (27.0)	7 (10.9)	1 (8.3)	1 (3.4)	0.036
Low	34 (54.0)	39 (60.9)	9 (75.0)	17 (58.6)	
Intermediate	12 (19.0)	18 (28.1)	2 (16.7)	11 (37.9)	
LR-PSS by MD Anderson					
Category 1	26 (41.3)	21 (32.8)	2 (16.7)	7 (24.1)	0.460
Category 2	32 (50.8)	33 (51.6)	8 (66.7)	17 (58.6)	
Category 3	5 (7.9)	10 (15.6)	2 (16.7)	5 (17.2)	

SLD - single lineage dysplasia, MLD - multi-lineage dysplasia, RS - ringed sideroblast, EB - excess of blast, BM - bone marrow, Hb – hemoglobin, ANC - absolute neutrophil counts, IPSS-R - Revised International Prognostic Scoring System, LR-PSS - lower risk prognostic scoring system.
*** median (range).**

Table S2. Patient characteristics according to the transfusion burden.

Variables	NTD	LTB	HTB	p-value
Number of patients	113	34	21	
Age, median year (range)	64 (20 - 92)	60 (28 - 86)	63 (39 - 77)	0.856
Gender				
Male	53 (46.9)	26 (76.5)	15 (71.4)	0.003
Female	60 (53.1)	8 (23.5)	6 (28.6)	
WHO classification				
SLD	18 (15.9)	7 (20.6)	4 (19.0)	0.426
MLD	6 (5.3)	2 (5.9)	0	
RS-SLD	81 (71.7)	21 (61.8)	14 (66.7)	
RS-MLD	3 (2.7)	2 (5.9)	1 (4.8)	
EB-1	4 (3.5)	0	2 (9.5)	
del(5q)	1 (0.9)	2 (5.9)	0	
BM blast% *	1.1 (0 - 9.5)	1.3 (0 - 3.2)	1.6 (0 - 6.9)	0.141
Hb (g/dL) *	9.6 (5.9 - 14.7)	8.3 (4.3 - 11.3)	7.4 (5.1 - 14.4)	< 0.001
ANC ($\times 10^3$/L) *	1.22 (0.14 - 10.06)	1.42 (0.39 - 4.75)	1.43 (0.15 - 3.88)	0.671
Platelet ($\times 10^9$/L) *	79 (12 - 604)	72 (4 - 484)	90 (4 - 485)	0.839
Cytogenetic risk by IPSS-R				
Very good	6 (5.3)	2 (5.9)	4 (19.0)	0.026
Good	103 (91.2)	27 (79.4)	16 (76.2)	
Intermediate	4 (3.5)	5 (14.7)	1 (4.8)	
Erythropoietin level (n = 78)				
< 200 U/L	34 (70.8)	10 (50.0)	6 (54.5)	0.292
200 - 500 U/L	7 (14.6)	3 (15.0)	1 (9.1)	
> 500 U/L	7 (14.6)	7 (35.0)	4 (36.4)	
Treatment				
No treatment	57 (50.4)	5 (14.7)	1 (4.8)	< 0.001
Anabolic steroids	39 (34.5)	20 (58.8)	6 (28.6)	
Erythroid stimulating agents	7 (6.2)	5 (14.7)	0	
Hypomethylating agents	10 (8.8)	4 (11.8)	14 (66.7)	
IPSS-R risk group				
Very low	23 (20.4)	3 (8.8)	0	0.017
Low	68 (60.2)	17 (50.0)	14 (66.7)	
Intermediate	22 (19.5)	14 (41.2)	7 (33.3)	
LR-PSS by MD Anderson				
Category 1	38 (33.6)	14 (41.2)	4 (19.0)	0.071
Category 2	65 (57.5)	13 (38.2)	12 (57.1)	
Category 3	10 (8.8)	7 (20.6)	5 (23.8)	

NTD - non-transfusion dependent, LTB - low transfusion burden, HTB - high transfusion burden, SLD - single lineage dysplasia, MLD - multi-lineage dysplasia, RS - ringed sideroblast, EB - excess of blast, BM - bone marrow, Hb - haemoglobin, ANC - absolute neutrophil counts, IPSS-R - Revised International Prognostic Scoring System, LR-PSS - lower risk prognostic scoring system.
*** median (range).**

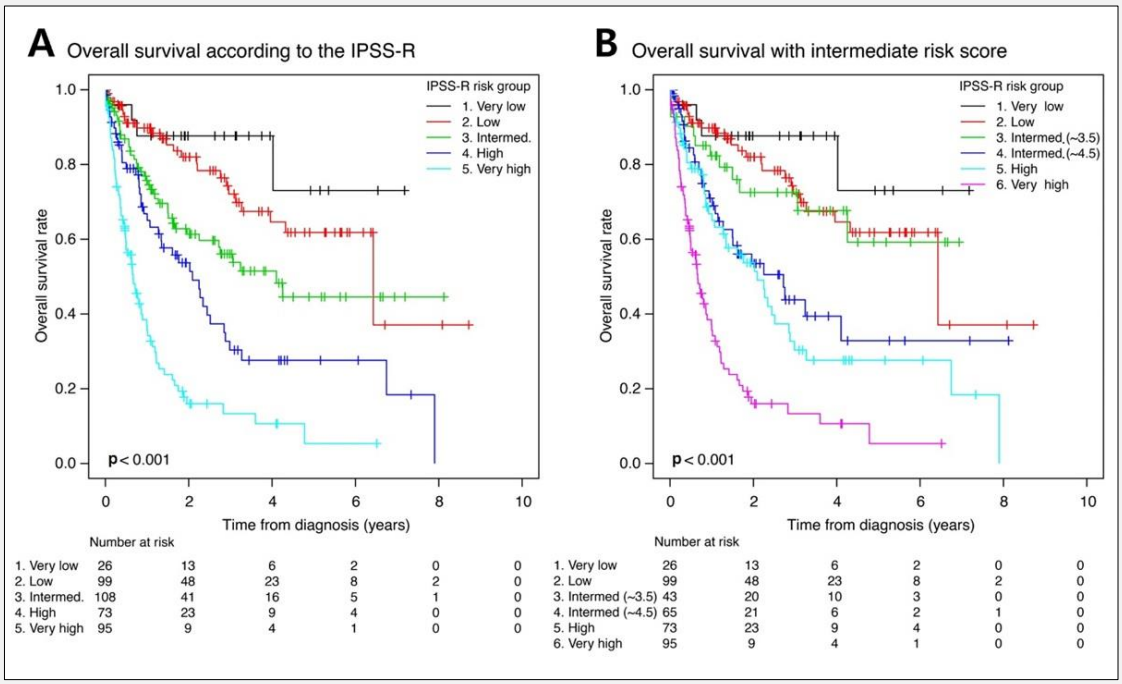

Figure S1. Overall survival rates according to the IPSS-R (n = 401).

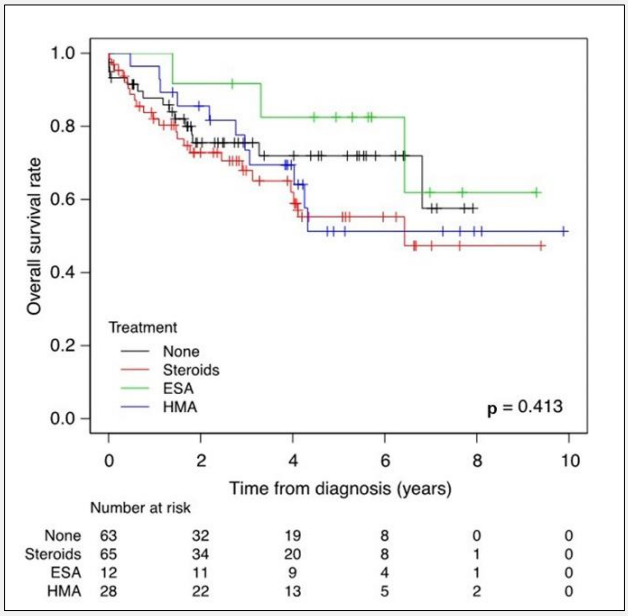

Figure S2. Overall survival rates according to the treatment options in patients with LR-MDS (n = 168).

ESA - erythroid stimulating agents, HMA - hypomethylating agents.
The 5-year overall survival rate was 71.9 ± 6.7% with no treatment, 55.2 ± 7.7% with anabolic steroids, 82.5 ± 12.6% with ESA, and 51.3 ± 11.1% with HMA.