LeukemiaNet
EUMDS REGISTRY

Hellenic Society of Hematology

The impact of Comorbidities and Infections in the course and prognosis of Myelodysplastic Syndromes

Argiris Symeonidis

Professor of Hematology

University of Patras, Greece

Recognition of prognostic factors is the key-point for treatment selection

Patient – related factors

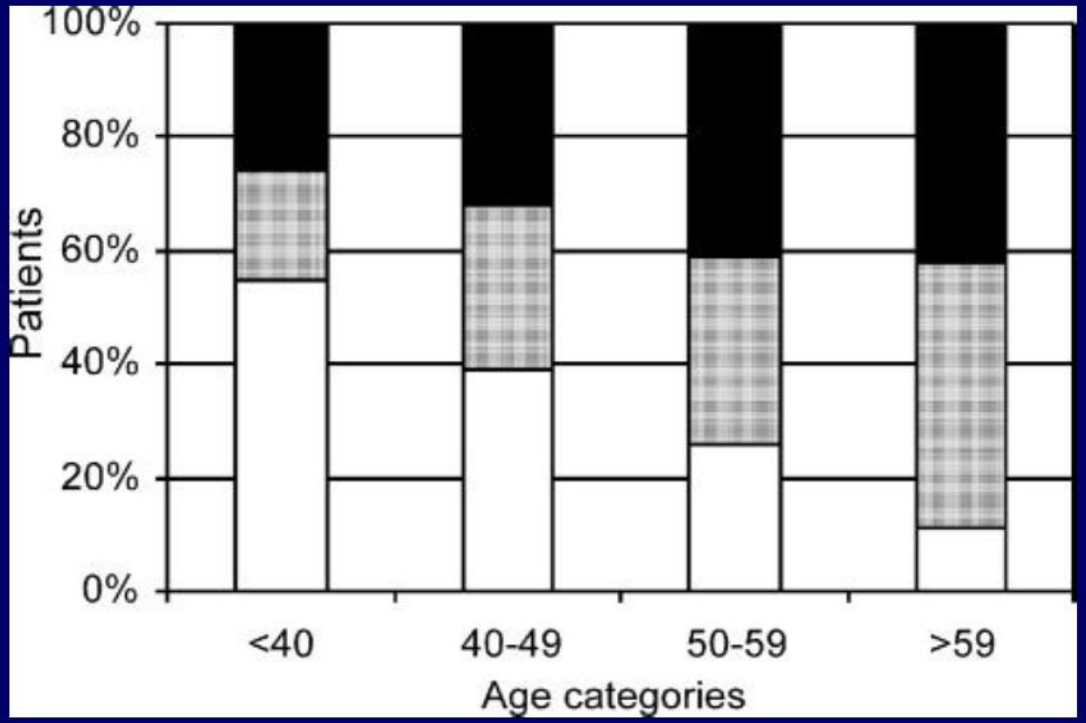
- Gender and age at initial Dx
- Performance Status, Frailty
- Number and type of comorbid conditions
- Previous exposure to cytotoxic agents
- Mental status, cognition
- Compliance to medical instructions

They both have the same age, 76 years

Disease – related factors

- Type of cytogenetic abnormalities
- BM blast cell percentage
- Multilineage dysplasia
- Marrow fibrosis
- Severity of anemia at presentation
- Transfusion dependence
- Baseline platelet count
- Serum LDH and β2-microglobulin levels
- Baseline serum ferritin and inflammatory markers' levels
- Response to ESA or AZA treatment

Relationship between age and comorbidities in MDS and AML

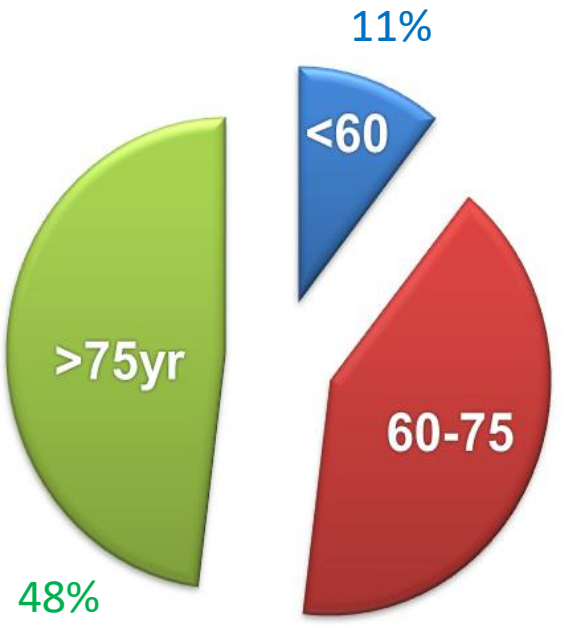


HCT-CI score 0, white area;
HCT-CI scores 1 to 2, gray area;
HCT-CI scores more than or equal to 3, black area.

AML

Sorror et al., Blood 2007;110:4606-4613

Age distribution of patients with MDS



Do comorbidities play an important role in prognosis?

Received: 20 February 2019 | Revised: 26 April 2019 | Accepted: 30 April 2019

DOI: 10.1111/ejh.13243

Annie M. Jacobsen[1] | Jenny N. Poynter[2,3] | Michaela R. Richardson[2] | Phuong L. Nguyen[4] | Betsy Hirsch[3,5] | Adina Cioc[6] | Michelle A. Roesler[2,3] | Erica D. Warlick[1]

WILEY European Journal of Haematology

Factors predicting early mortality after new diagnosis of myelodysplastic syndrome: A population-based study

TABLE 2 Comparison of clinical characteristics in MDS patients who did and did not die within 1 y of diagnosis

Characteristic	Survived < 1 y N (%)	Survived ≥ 1 y N (%)	Unadjusted OR (95% CI)	*P*-value[b]	Multivariable adjusted[a] OR (95% CI)	*P*-value[b]
Total	85	314				
Treatment						
Hypomethylating agent	25 (30.1)	43 (14.0)	**2.72 (1.50-4.95)**	**0.001**	1.24 (0.55-2.78)	0.61
Transplant	10 (12.1)	36 (11.7)	1.27 (0.58-2.75)	0.55	0.57 (0.17-1.94)	0.37
Supportive care only	41 (49.4)	192 (62.5)	*Ref*		*Ref*	
Comorbidities						
0-1	28 (32.9)	140 (44.7)	*Ref*		*Ref*	
2-3	46 (54.1)	119 (38.0)	**1.95 (1.15-3.31)**	**0.01**	**2.14 (1.08-4.22)**	**0.03**
≥4	11 (12.9)	54 (17.3)	1.03 (0.48-2.20)	0.95	0.74 (0.28-1.97)	0.55
Cytogenetics						
Normal	14 (17.5)	153 (51.5)	*Ref*		*Ref*	
Abnormal	66 (82.5)	144 (48.5)	**5.04 (2.71-9.37)**	**<0.0001**	**3.36 (1.52-7.46)**	**0.003**
Complex karyotype[c] (≥ 3 abnormalities)	33 (38.8)	22 (7.0)	**8.03 (4.37-14.75)**	**<0.0001**	**3.48 (1.51-7.99)**	**0.003**

original article

Annals of Oncology 21: 114–119, 2010
doi:10.1093/annonc/mdp258
Published online 15 July 2009

Comorbidity as prognostic variable in MDS: comparative evaluation of the HCT-CI and CCI in a core dataset of 419 patients of the Austrian MDS Study Group

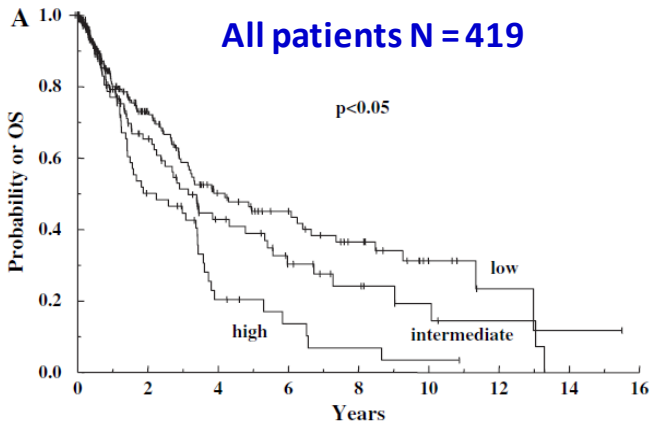
W. R. Sperr[1*], F. Wimazal[1], M. Kundi[2], C. Baumgartner[1], T. Nösslinger[3], A. Makrai[3], R. Stauder[4], O. Krieger[5], M. Pfeilstöcker[1,6] & P. Valent[1,6]

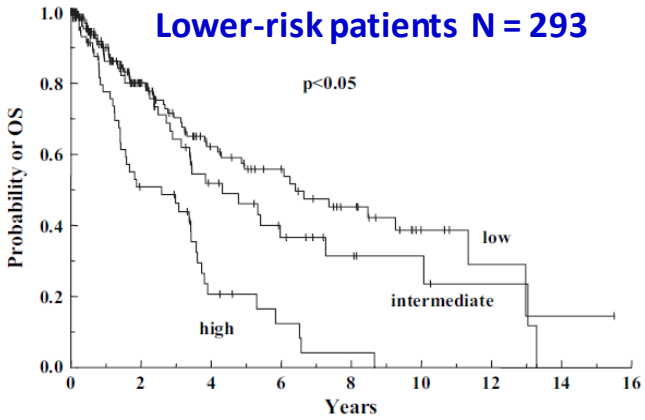
FAB	*n*	Age median (range)	Female : male	WBC, G/l median (range)	Hb, g/dl median (range)	Plt, G/l median (range)	IPSS, *n*			
							Low	Int-1	Int-2	High
RA	128	70 (24–88)	61 : 67; 1 : 1.1	3.8 (1.3–11.6)	10.2 (3.6–15.9)	135.5 (3–680)	67	58	3	0
RARS	94	73 (25–89)	40 : 54; 1 : 1.4	5.0 (1.2–9.7)	10.0 (5.2–13.6)	226 (21–946)	59	33	2	0
RAEB	109	72 (36–89)	52 : 57; 1 : 1.1	2.8 (0.5–76.5)	9.8 (5.3–15.4)	81 (10–670)	0	49	51	9
RAEB-t	63	65 (27–85)	18 : 35; 1 : 1.3	4.2 (0.7–107.5)	9.3 (5.4–12.9)	76 (12–390)	1[a]	6	18	38
CMML	25	75 (52–91)	10 : 15; 1 : 1.5	5.6 (1.7–11.8)	10.9 (6.7–14.8)	90 (20–216)	8	12	5	0
All patients	419	71 (24–91)	191 : 228; 1 : 1.2	4.0 (0.5–107.5)	9.8 (3.6–15.9)	118 (3–946)	135	158	79	47

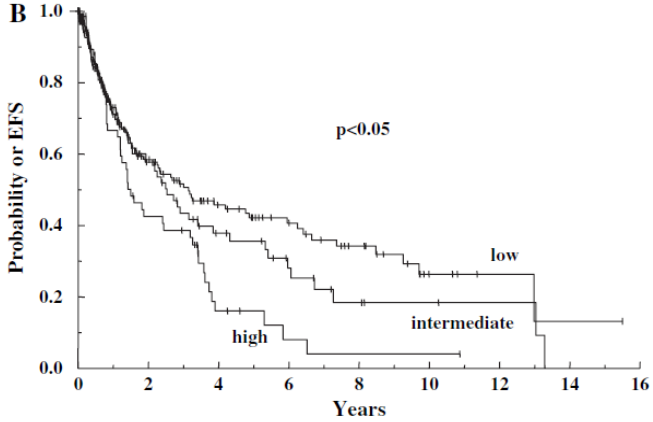
IPSS	OS	AFS	EFS	Patients (*n*)
Low	6.65	n.r.	6.52	135
Int-1	2.83	9.71	2.28	158
Int-2	2.03	1.52	1.06	79
High	0.76	0.88	0.37	47
P value	<0.05	<0.05	<0.05	

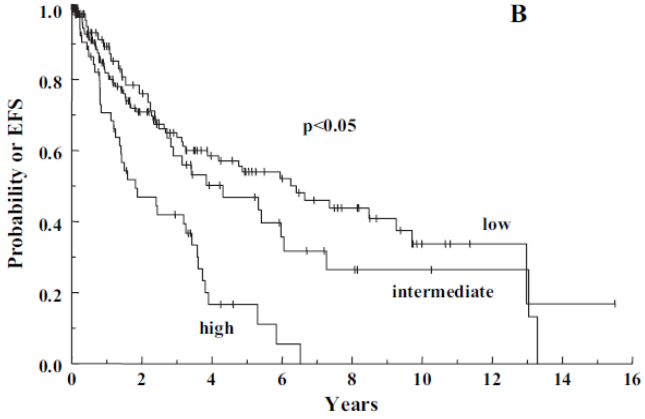
IPSS, International Prognostic Scoring System; OS, overall survival; AFS, AML-free survival; EFS, event-free survival; n.r., not reached yet.

Comorbidity as a prognostic variable in MDS









- Both indeces, Charlson's and HTC-CI could be applied and had prognostic value
- Charlson's CI was predictive for OS only, whereas HTC-CI was also predictive for EFS and AML-free survival
- HTC-CI was also predictable for OS and EFS for patients with IPSS-low and Int-1 risk (lower risk MDS)

Sperr et al. Ann Oncol. 21: 114, 2010

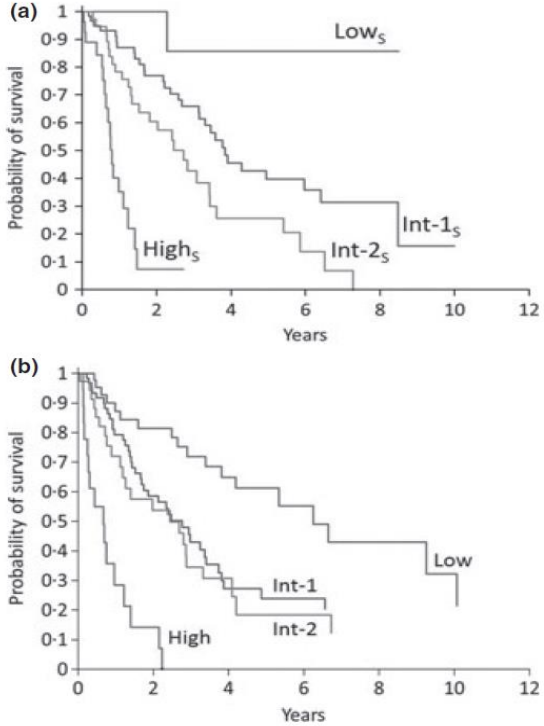
Proposed score for survival of patients with myelodysplastic syndromes

Eur J Clin Invest 2013; 43 (11): 1120–1128

Wolfgang R. Sperr*, Michael Kundi†, Friedrich Wimazal‡, Thomas Nösslinger§, Anabel Schönmetzler-Makrai§, Reinhard Stauder¶, Otto Krieger**, Judith Neukirchen††, Ulrich Germing††, Michael Pfeilstöcker§,‡‡ and Peter Valent*,‡‡

Table 3 Survival score

Prognostic variable	Score value 0	0.5	1	1.5	2
IPSS Points	0	0.5	1	1.5	≥ 2
Ferritin (ng/mL)	<900		≥ 900		
Age (year)	<70	70–79		≥ 80	
HTC-CI	Low/medium	High			



- **Independent prognostic significance for age, ferritin, HTC-CI, Cytogenetic group*, BM blasts*, Hb*, ANC*, platelets* (later included in the IPSS-R)**
- **Proposal for a new prognostic tool with IPSS, Ferritin, Age and HTC-CI, which was superior to IPSS**

Do all types of comorbidity have the same impact on prognosis?

- Thyroid diseases have equal impact as cardiac diseases?
- Which comorbidity has major impact and should be taken into consideration more seriously?
- Is diabetes on the same degree of importance in all patients?
- Can we quantify the impact of each comorbidity or of the same comorbid condition in different patients?
- How can we evaluate and quantify the severity of comorbid conditions?

Risk stratification based on both disease status and extra-hematologic comorbidities in patients with myelodysplastic syndrome

Matteo G. Della Porta,[1] Luca Malcovati,[1] Corinna Strupp,[2] Ilaria Ambaglio,[1] Andrea Kuendgen,[2] Esther Zipperer,[2] Erica Travaglino,[3] Rosangela Invernizzi,[3] Cristiana Pascutto,[1] Mario Lazzarino,[1] Ulrich Germing,[2] and Mario Cazzola[1]

Table 1. Clinical and hematologic characteristics of the Italian and German cohorts of MDS patients classified according to the 2008 WHO criteria.

Characteristic	Learning cohort (Pavia, Italy)	Validation cohort (Duesseldorf, Germany)	*P*
Number of patients	840	504	-
Median age (range)	66 (18-92)	73 (18-92)	<0.001
Sex (male/female)	504/336	289/215	NS
WHO classification:			
RCUD/RARS/MDS del(5q)	270 (32%)	96 (19%)	<0.001
RCMD	291 (35%)	232 (46%)	
RAEB-1	118 (14%)	76 (15%)	
RAEB-2	161 (19%)	100 (20%)	
Informative cytogenetics	632/840 (75%)	261/504 (52%)	-
Transfusion-dependency*	291/840 (35%)	215/489 (44%)	<0.001
IPSS risk**			
Assessable cases/total cases (%)	632/840 (75%)	261/504 (52%)	-
Low	227/632 (36%)	73/261 (28%)	0.013
Intermediate-1	259/632 (41%)	115/261 (44%)	
Intermediate-2	117/632 (19%)	50/261 (19%)	
High	29/632 (5%)	23/261 (9%)	
WPSS risk***			
Assessable cases/total cases (%)	632/840 (75%)	246/489 (50%)	
Very low	145/632 (23%)	27/246 (11%)	<0.001
Low	170/632 (27%)	61/246 (25%)	
Intermediate	112/632 (18%)	58/246 (24%)	
High	172/632 (27%)	74/246 (30%)	
Very high	33/632 (6%)	26/246 (10%)	

Comorbidity	HR obtained through a multivariable Cox's survival analysis with NLD as an outcome	Variable weighted score (to be taken into account if the specific comorbidity is present)
Cardiac disease	3.57 (*P*<0.001)	2
Moderate-to-severe hepatic disease	2.55 (*P*=0.01)	1
Severe pulmonary disease	2.44 (*P*=0.005)	1
Renal disease	1.97 (*P*=0.04)	1
Solid tumor	2.61 (*P*<0.001)	1

MDS-CI risk	Sum of individual variable scores	Proportion of patients in the learning cohort belonging to the risk group (%)
Low risk	0	546/840 (65%)
Intermediate risk	1-2	244/840 (29%)
High risk	>2	50/840 (6%)

5 groups of comorbidities, were independently associated with non-leukemic death:

- **Cardiac**
- **moderate/severe Liver**
- **Pulmonary**
- **Renal**
- **Neoplastic (disease)**

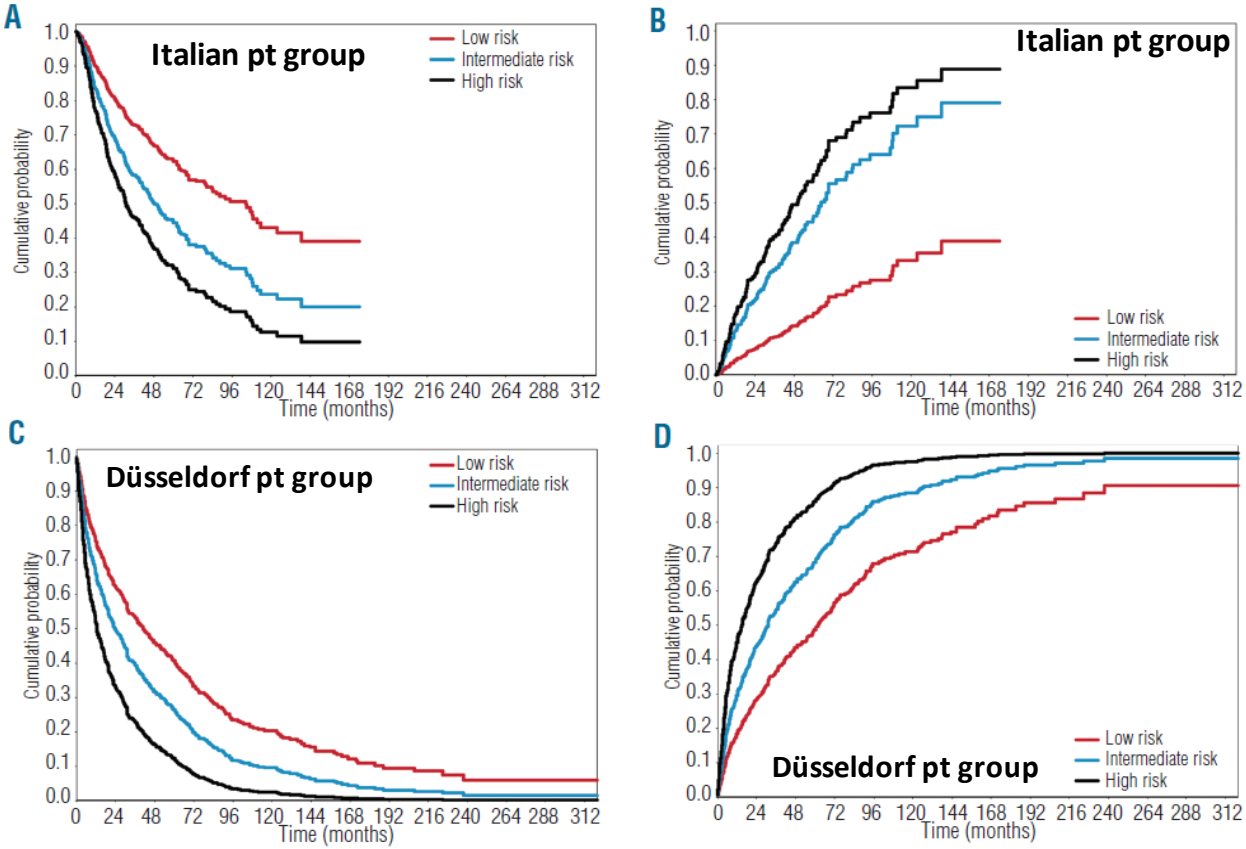
Haematologica 96(3): 441-49, 2011

Risk stratification for MDS based also on comorbidities

Table 2. Definition of comorbidities according to Sorror *et al.*,[21] and their prevalence in the Pavia learning cohort of MDS patients.

Comorbidity	Definition	Prevalence	
Cardiac	Arrhythmia* Heart valve disease** Coronary artery disease *** or myocardial infarction Congestive heart failure or ejection fraction ≤50%	7% 2% 8% 19%	25%
Cerebrovascular	Transient ischemic attack and/or ischemic or hemorrhagic cerebrovascular accident	5%	
Mild to moderate pulmonary	DLCO and/or FEV1 66%-80% or dyspnea on moderate or slight activity	3%	
Severe pulmonary	DLCO and/or FEV1 ≤65% or dyspnea at rest or requires oxygen	2%	
Mild hepatic ****	Chronic hepatitis, persistent bilirubin > ULN to 1.5 x ULN or AST/ALT > ULN to 2.5 x ULN	14%	
Moderate to severe hepatic ****	Cirrhosis, fibrosis, persistent bilirubin > 1.5 x ULN or AST/ALT > 2.5 x ULN	3%	
Renal	Persistent creatinine > 2 mg/dL, renal dialysis, or renal transplant	4%	
Solid tumor	Malignancy at any time point in the patient's history, excluding non-melanoma skin cancer	10%	
Rheumatological	One or more of the following conditions: systemic lupus erythematosus, rheumatoid arthritis, polymyositis, mixed connective tissue disease, polymyalgia rheumatica	2%	
Gastrointestinal	One or more of the following conditions: Crohn's disease, ulcerative colitis, or peptic ulcer requiring treatment	6%	
Diabetes	Diabetes requiring treatment with insulin or oral hypoglycemics	11%	
Endocrine	One or more of the following conditions: thyroid disorders, adrenal disorders, parathyroid gland disorders, pituitary gland disorders, or hypogonadism	5%	
Obesity	Body mass index >35 kg/m^2	2%	
Psychiatric	Depression or anxiety requiring psychiatric counseling or treatment	2%	

Independent prognostication of MDS-specific CI for OS and non-leukemic death in both cohorts



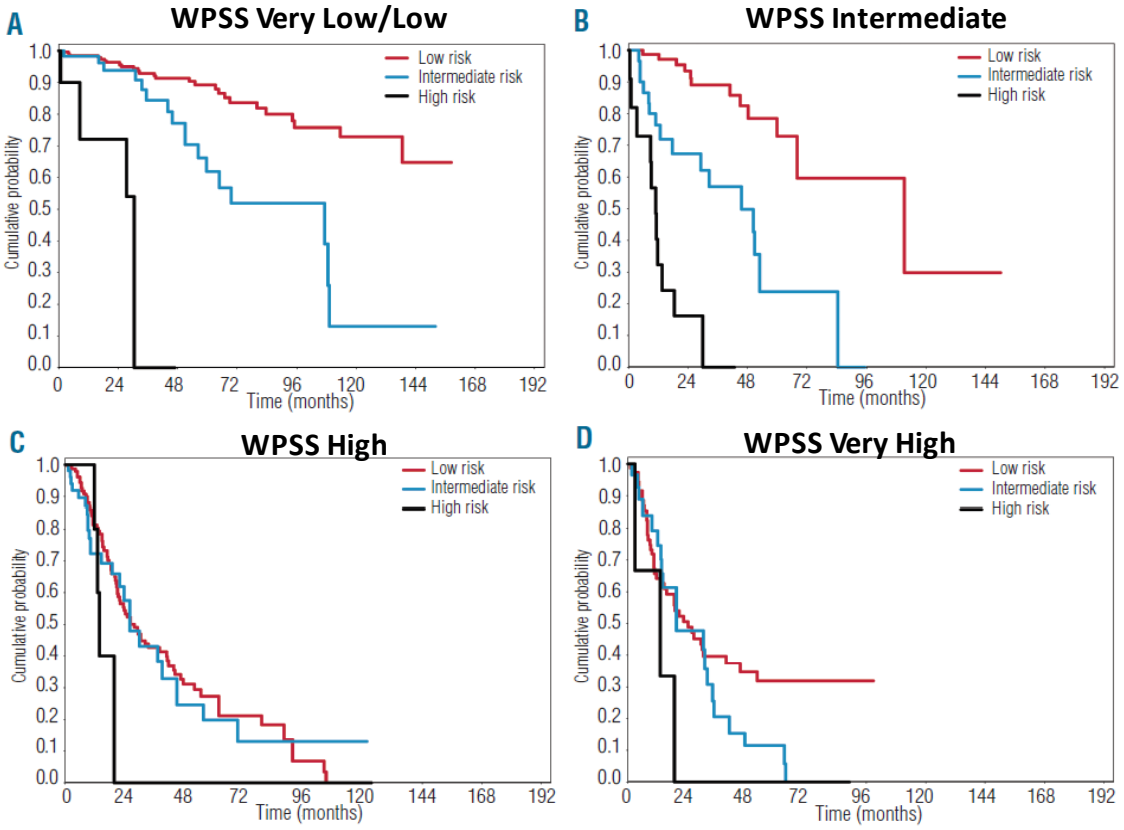
The MDS-specific CI could effectively and independently predict for:

- **Overall survival and**
- **non-leukemic death**

in both patient cohorts

Della Porta M et al.
Haematologica 96(3): 441-49, 2011

Complementary prognostic significance of MDS-CI over the classical prognostic scoring systems for MDS



- MDS-CI was capable to add prognostic value in all the IPSS-defined prognostic categories of patients
- The same was true with WPSS which can be applied at any time point in the disease course
- Thus coupling of MDS-CI to WPSS represents a dynamic prognostic tool with high prognostic value, applicable at any time point on MDS pts

Della Porta M et al.
Haematologica 96(3): 441-49, 2011

The risk of progression to higher risk category of comorbidities is increased among transfusion-dependent patients

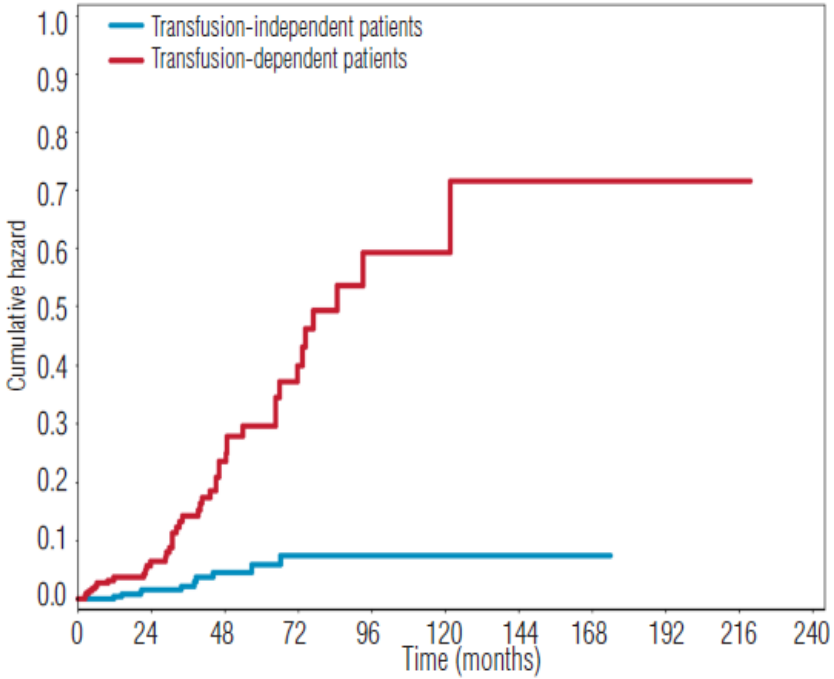


Figure 2. Risk of progression to a higher MDS-CI category during the course of the disease. Cumulative hazard of MDS-CI progression in the Italian cohort according to the presence or absence of transfusion dependency.

Della Porta et al. Haematologica 2011; 96(3): 441-449

LEUKEMIA & LYMPHOMA, 2016
http://dx.doi.org/10.1080/10428194.2016.1267350

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE: CLINICAL

The incorporation of comorbidities in the prognostication of patients with lower-risk myelodysplastic syndrome*

Jose F. Falantes, Francisco J. Márquez-Malaver, Teresa Knight, Cristina Calderón-Cabrera, María L. Martino, Jose González, Isabel Montero, Ildefonso Espigado and Jose A. Pérez-Simón

Probability of Non-Leukemic Death at Dx

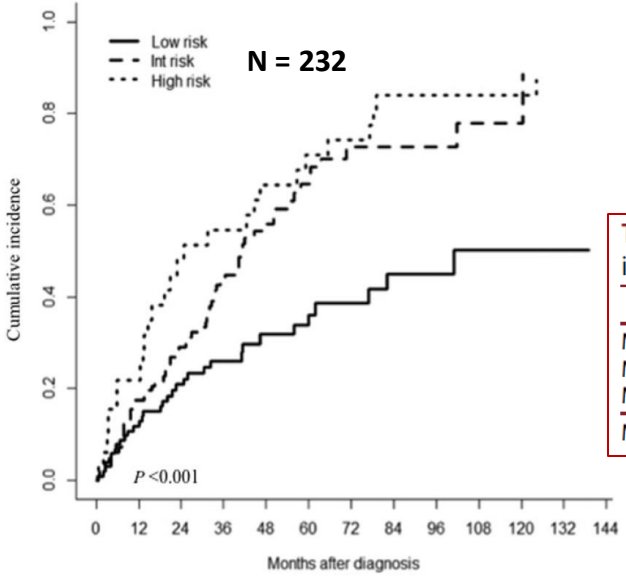
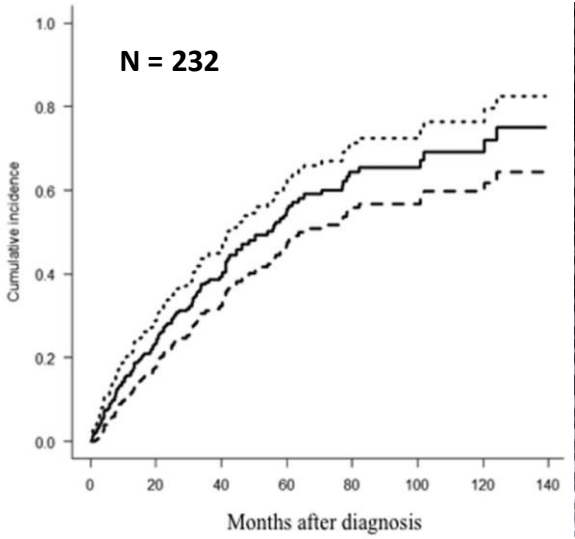


Table 3. Cumulative incidence of non-leukemic death according to MDS-CI (all patients).

	12 months	24 months	36 months	48 months
MDS-CI low risk	11.9%	20.9%	26.1%	31.9%
MDS-CI int risk	17.5%	29%	43.7%	54.3%
MDS-CI high risk	21.9%	48.1%	54.6%	64.4%

MDS-CI: myelodysplastic syndromes comorbidity index.

Probability of Non-Leukemic Death over time



Association of Comorbidities With Overall Survival in Myelodysplastic Syndrome: Development of a Prognostic Model

VOLUME 29 · NUMBER 16 · JUNE 1 2011

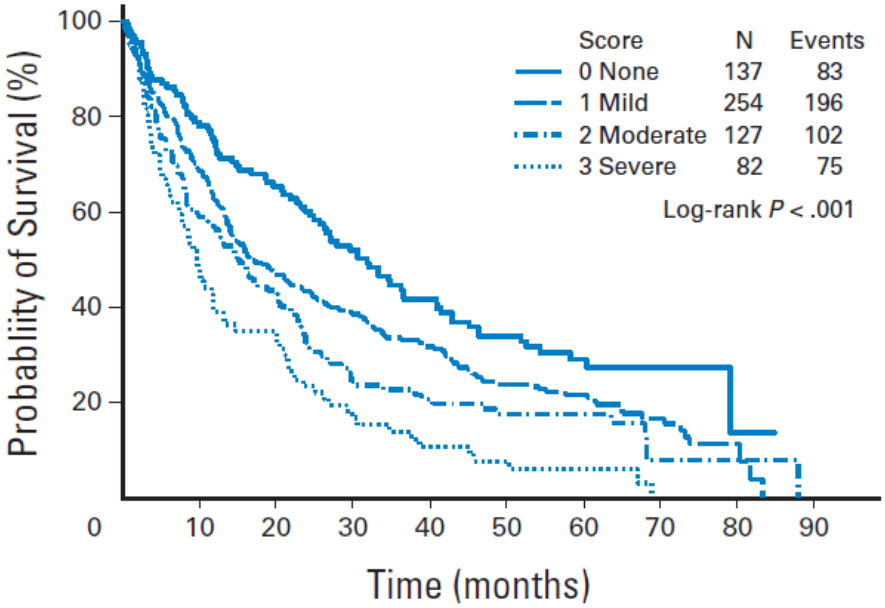
JOURNAL OF CLINICAL ONCOLOGY

Kiran Naqvi, Guillermo Garcia-Manero, Sagar Sardesai, Jeong Oh, Carlos E. Vigil, Sherry Pierce, Xiudong Lei, Jianqin Shan, Hagop M. Kantarjian, and Maria E. Suarez-Almazor

Table 1. Patient Comorbidities

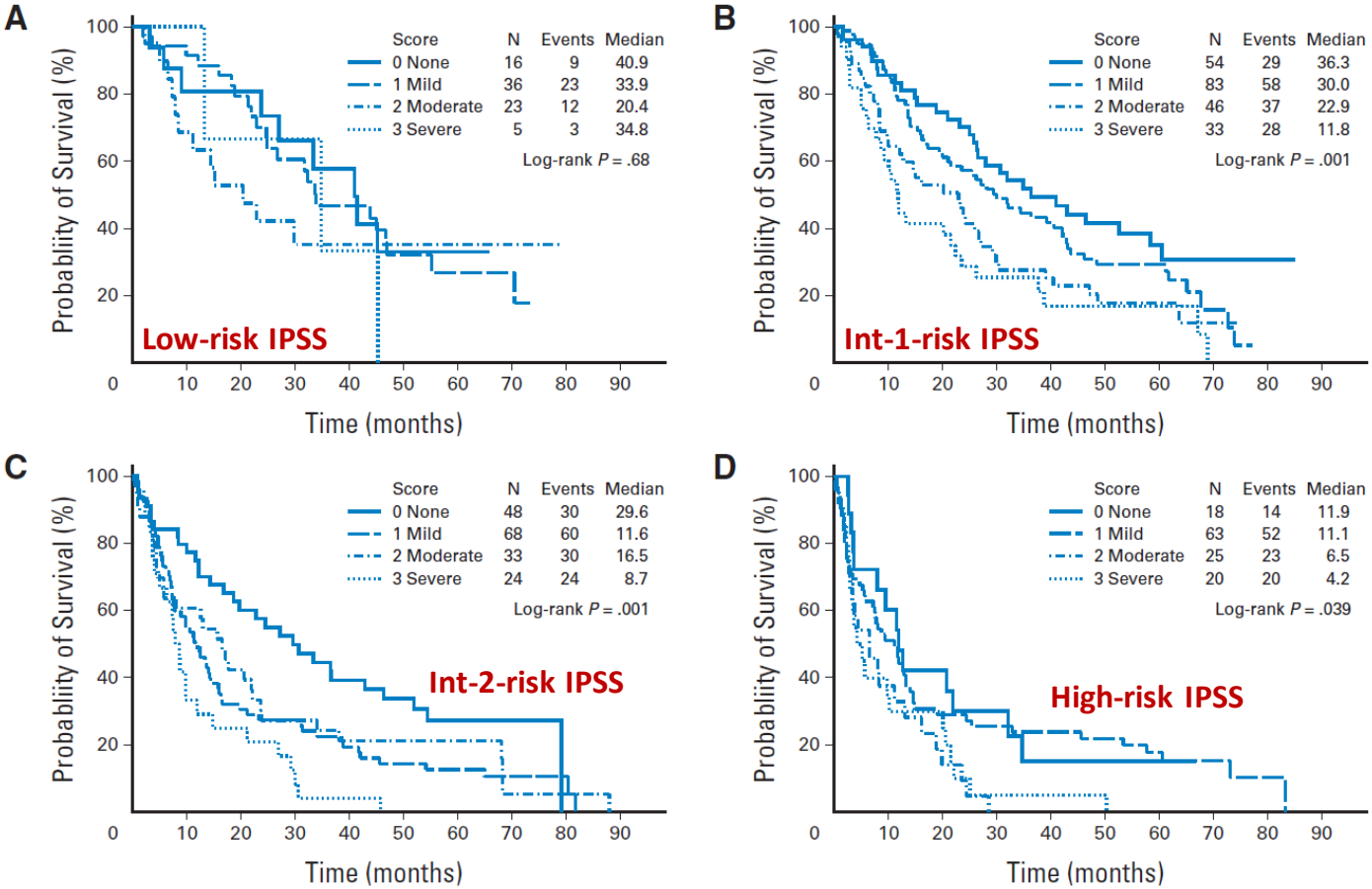
Comorbidity	No.	%
ACE-27 score		
None, 0	137	22.8
Mild, 1	254	42.3
Moderate, 2	127	21.2
Severe, 3	82	13.7
System		
Cardiovascular	328	54.7
Endocrine	97	16.2
GI	40	6.7
Immunologic	1	0.2
Malignancy	168	28.0
Neurologic	35	5.8
Obesity	1	0.2
Psychiatric	48	8.0
Renal	14	2.3
Respiratory	53	8.8
Rheumatologic	17	2.8
Substance abuse	32	5.3

Abbreviation: ACE-27, Adult Comorbidity Evaluation-27.



- **ACE-27 score provides a useful prognostic categorization of MDS patients and can be applied**

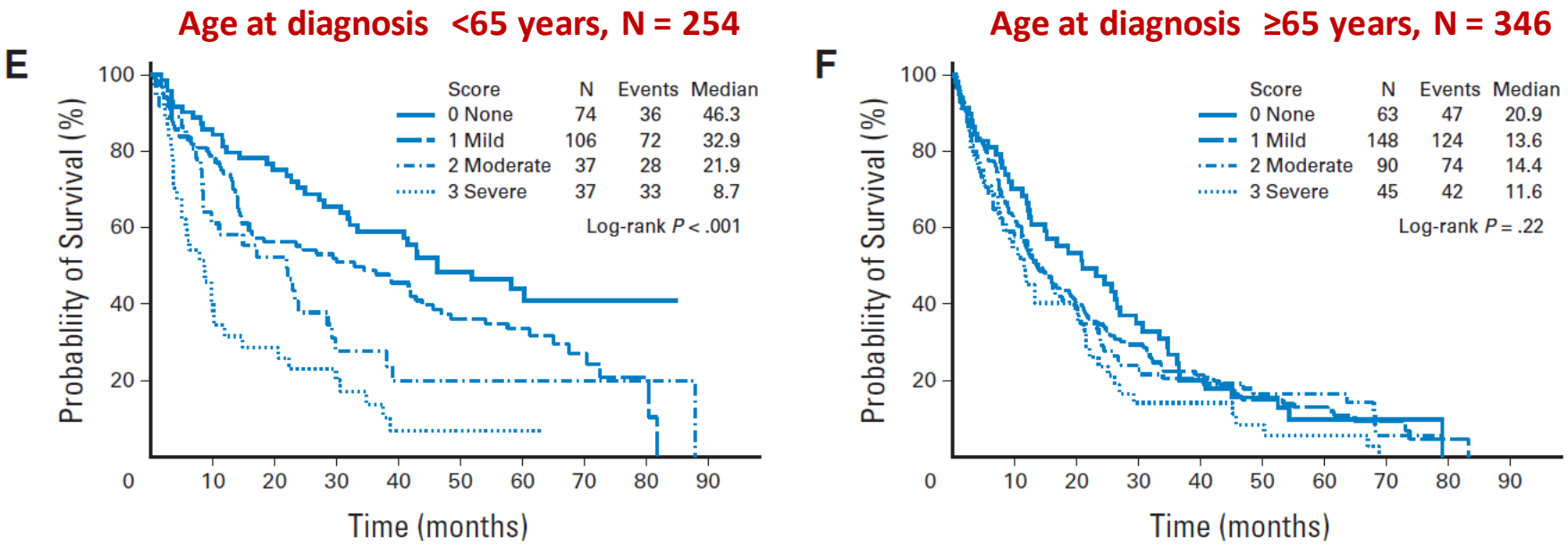
Usefulness of ACE-27 as a prognostic tool in MDS



- **ACE-27 (Adult comorbidity evaluation 27) can stratify well patients with Int-1 and Int-2 IPSS, and roughly patients with High IPSS**
- **ACE-27 cannot be a useful prognostic tool for patients with Low IPSS**

Naqvi et al. JCO 29:2240, 2011

Usefulness of ACE-27 as a prognostic tool in MDS: The role of age



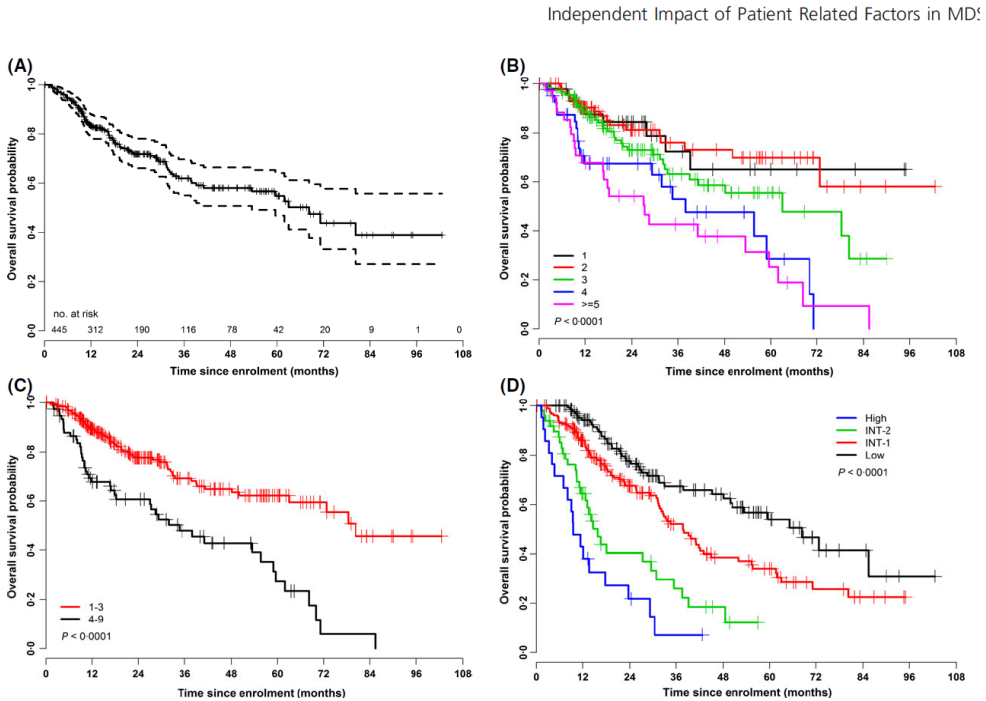
- **Regarding overall survival in MDS, ACE-27 is a very useful prognostic tool for patients younger than 65 years but has not prognostic power for older patients**

Naqvi et al. JCO 29:2240, 2011

bjh research paper

Patient-related factors independently impact overall survival in patients with myelodysplastic syndromes: an MDS-CAN prospective study

Buckstein R et al: *British Journal of Haematology*, 2016, **174**, 88–101

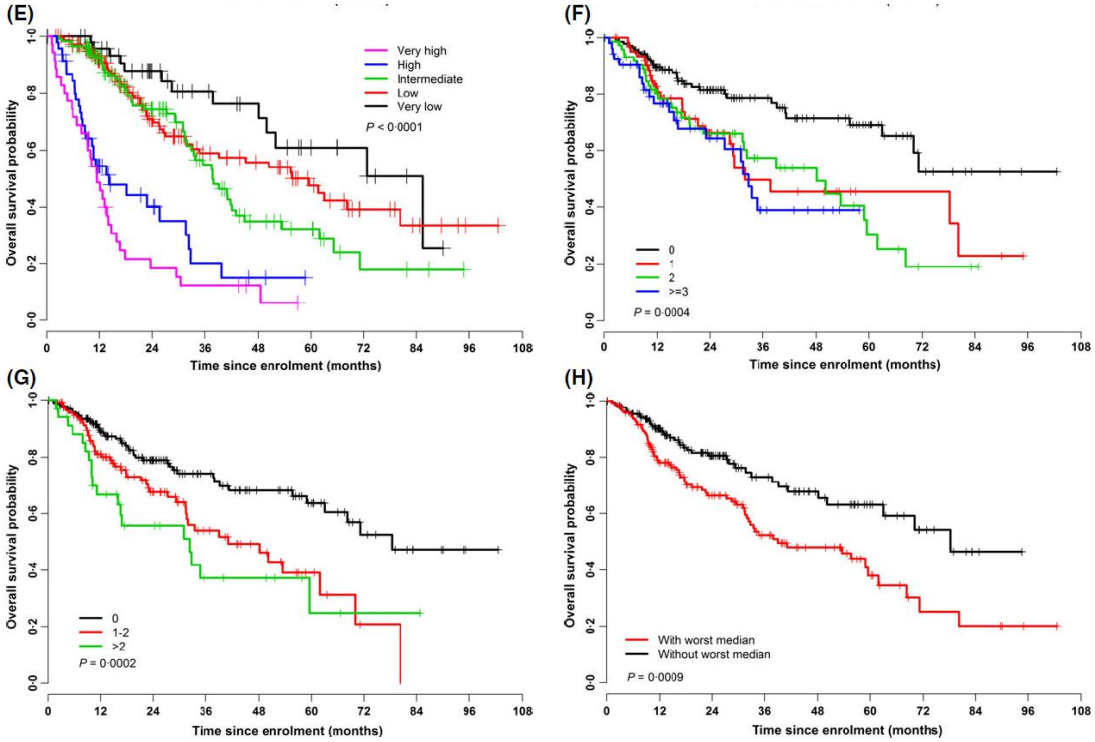


- **A: Overall survival of all patients (median, 95% C.I.)**
- **B: Survival according to Frailty score**
- **C: Survival by Frailty score (1-3 vs >3)**
- **D: Survival according to IPSS**

bjh research paper

Patient-related factors independently impact overall survival in patients with myelodysplastic syndromes: an MDS-CAN prospective study

Buckstein R et al: *British Journal of Haematology*, 2016, **174**, 88–101



- **E: Overall survival according to IPSS-R**
- **F: Survival according to Charlson's comorbidity Index**
- **G: Survival according to MDS-specific Comorbidity Index**
- **H: Survival according to Lawton-Brody disability score**

Integrating patient-centered factors in the risk assessment of MDS

Rena J. Buckstein

Odette Cancer Center, Sunnybrook Health Sciences Center, Toronto, ON, Canada

- Patient-related factors add prognostic value to all prognostic systems
- Besides the various ***co-morbidity indexes***, ***frailty*** or ***geriatric assessment*** should also be applied at every critical point in the course of an MDS
- These assessments should be combined with ***disease-based risk factors*** and with ***QoL tools*** to create ***combined-modality prognostic tools***
- All the above tend to **quantify and rationalize** the individual-based treatment approaches in patients with MDS

No doubt infections is a major concern in MDS

Mediterranean Journal of Hematology and Infectious Diseases

Review Article

Infections in Myelodysplastic Syndrome in Relation to Stage and Therapy

Giuseppe Leone and Livio Pagano Mediterr J Hematol Infect Dis 2018; 10; e2018039

Table 1. Prevalence of Infectious complications in the MDS Follow-up Cohort of the USA from Medicare Standard Analytic Files (SAF). Adapted from Goldeberg et Al.[1] *J Clin Oncol 2010.*

	MDS		Overalll SAF Medicare Population		
No. of Subjects	512		1,379,185		
Characteristics of Infect. Complications	No	%	No	%	*P*
Sepsis	115	22.5	84,530	6.1	<.001
Bacteremia	80	15.6	110,904	8.0	<.001
Fungal Infection	49	9.6	66,129	4,8	<.001
Cellulitis	158	30.9	269,615	19.5	<.001
Renal Infections	18	3.5	19,860	1.4	<.001
Intestinal Infections	38	7.4	47,833	3.5	<.001
Pneumonia	204	39.8	272,487	19,8	<.001

Infections in Myelodysplastic Syndrome in Relation to Stage and Therapy

Giuseppe Leone and Livio Pagano Mediterr J Hematol Infect Dis 2018; 10; e2018039

Table 2. Risk Factors for infections in MDS High-risk. += risk factor; ± =no risk factor.

Risk Factors	
Male gender	± ± ± ±
Age	± ± + ± +
High risk/ Blast count/ poor cytogenetics	+ + +
Neutropenia	+ + + ±
Thrombocytopenia	+ ± + ±
COPD	+
Comorbidities	+ ±
Diabetes	±
Hypoalbuminemia	+
Previous Chemotherapy	+ + ±
Hypomethylating agents	± ± +
Intensive Chemotherapy	++
Iron Overload	+ + ± +
Anemia/transfusion dependence	+ + + ±
Antimicrobial prophylaxis	+ + ± ±

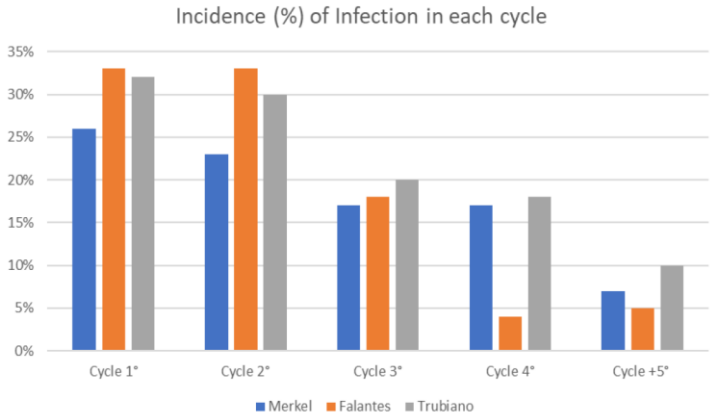
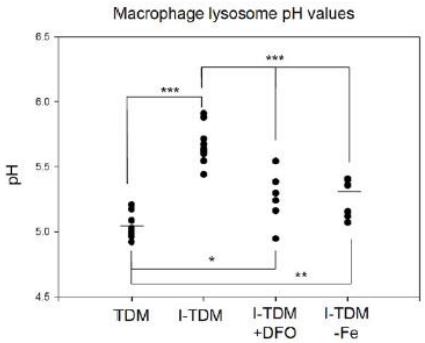


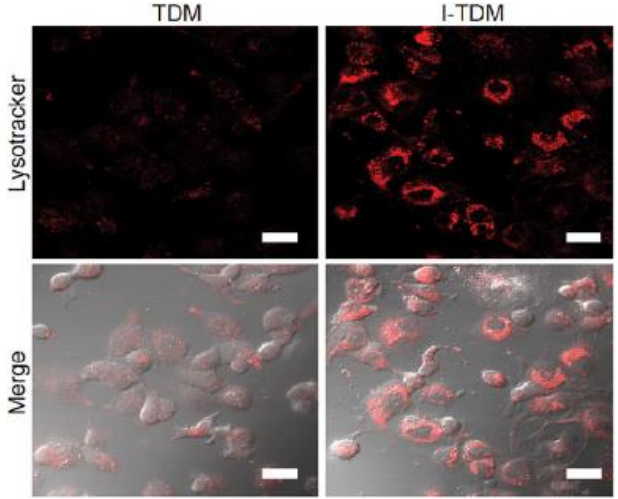
Table 3. The rate of infections related to the number of cycles.

Author	Patients treated	AZA N° Cycles	N° Infections, %	N° Deaths from Infections, %
Merkel (8)	184	928	153 (16.48)	30(24.39)
*Lorenzana (63)	76	283	59 (20.08)	12 (20.33)
Trubiano (62)	68	884	124 (14.02)	16(12.90)
^Falantes (60)	64	523	72 (13.76)	2
Shuck (59)	77	614	81(13,19)	6 (7.79)
Ofran 1 (58)	106	106	36 (33.96)	
Ofran 2 (58)	67	67	10(14.9)	

Factors predisposing to infections in patients with MDS

- Underlying diseases / conditions (DM, COPD, Renal failure etc)
- Neutropenia, functional neutrophil defects
- Impaired cellular immunity
- Permanent central venous catheters, Foley catheters
- Prolonged in hospital stay, low mobilization, prolonged bedding
- Extended prophylactic use of antibiotics
- Iron overload (?)
- Treatment induced factors (Chemotherapy, HMAs, steroids, immunosuppressive treatment etc)





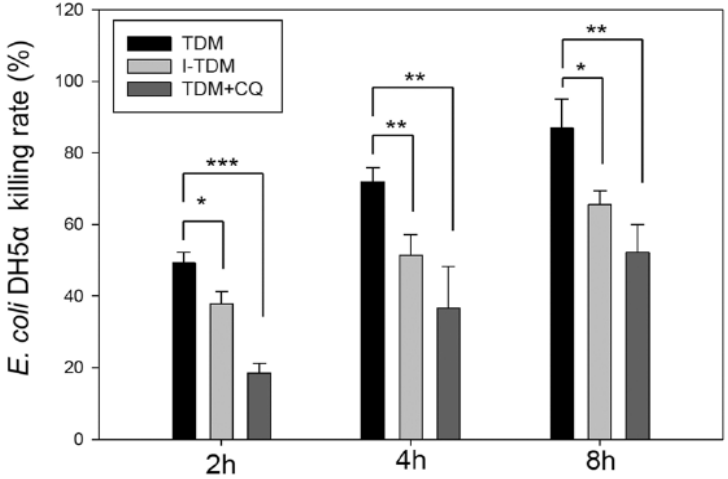
Iron loaded macrophages exhibit lysosomal dysfunction, with increased intralysosomal pH, reduced bactericidal activity and relative proportional lysosomal hyperplasia per cell

PLOS | ONE

RESEARCH ARTICLE

Chronic Iron Overload Results in Impaired Bacterial Killing of THP-1 Derived Macrophage through the Inhibition of Lysosomal Acidification

Jun-Kai Kao[1,2], Shih-Chung Wang[2], Li-Wei Ho[1,2], Shi-Wei Huang[3], Shu-Hao Chang[4], Rei-Cheng Yang[2], Yu-Yuan Ke[5], Chun-Ying Wu[6], Jiu-Yao Wang[7,8]*, Jeng-Jer Shieh[1,3,9]*



Dose-dependent reduction of bactericidal activity against E.coli and Ps. Aeruginosa as a result of lysosomal dysfunction, impaired redox potential, pH increase, impaired cathepsine activity and reduced autophagy

What kind of infections MDS patients usually develop – I.

Table 2. Classification of 111 pulmonary infection episodes according to results of the microbiological and radiological diagnostic work-up

Classification of pulmonary infection	Number of cases (%)
Pulmonary infection of unknown origin	71 (64.0)
Pulmonary invasive fungal disease	27 (24.3)
Proven	0
Probable aspergillosis*	13
Possible	13
Pneumocystis jiroveci pneumonia	1
Bacterial pulmonary infection	11 (9.9)
Streptococcus pneumoniae	4
Klebsiella pneumoniae	2
Escherichia coli	2
Pseudomonas aeruginosa	1
Staphylococcus spp	2
Influenza pulmonary infection	2 (1.8)

Latagliata R et al: Hematological Oncol. Epub 31.12.2019

What kind of infections MDS patients usually develop – II.

Table 3 Microbiologically Confirmed Infections

Type of Infection	n	Pathogen	n
Bacterial	41		
		Gram-positive bacteria	20
		Coagulase-negative *Staphylococcus*	8
		Staphylococcus aureus	1
		Enterococcus spp.	8
		Clostridium difficile	3
		Gram-negative bacteria	20
		Escherichia coli	8
		Klebsiella pneumoniae	5
		Enterobacter spp.	2
		Proteus mirabilis	1
		Acinetobacter baumannii	2
		Pseudomonas aeruginosa	1
		Stenotrophomonas maltophilia	1
		Mycobacterium kansasii	1
Fungal		14	
Proven	4	*Aspergillus fumigates*	2
		Candida tropicalis	2
Probable	10		
Viral		0	

Madry K et al. *Clinical Lymphoma, Myeloma & Leukemia,* Vol. 19, No. 5, 264-74 © 2019

Predictive Model for Infection Risk in Myelodysplastic Syndromes, Acute Myeloid Leukemia, and Chronic Myelomonocytic Leukemia Patients Treated With Azacitidine; Azacitidine Infection Risk Model: The Polish Adult Leukemia Group Study

Krzysztof Mądry,[1] Karol Lis,[1] Przemysław Biecek,[2] Magda Młynarczyk,[2] Jagoda Rytel,[1] Michał Górka,[1] Piotr Kacprzyk,[1] Magdalena Dutka,[3] Marek Rodzaj,[4] Łukasz Bołkun,[5] Dorota Krochmalczyk,[6] Ewa Łątka,[6] Joanna Drozd-Sokołowska,[1] Anna Waszczuk-Gajda,[1] Wanda Knopińska-Posłuszny,[7] Anna Kopińska,[8] Edyta Subocz,[9] Anna Masternak,[10] Renata Guzicka-Kazimierczak,[11] Lidia Gil,[12] Rafał Machowicz,[1] Jarosław Biliński,[1] Sebastian Giebel,[13] Tomasz Czerw,[13] Jadwiga Dwilewicz-Trojaczek[1]

Clinical Lymphoma, Myeloma & Leukemia, Vol. 19, No. 5, 264-74 © 2019

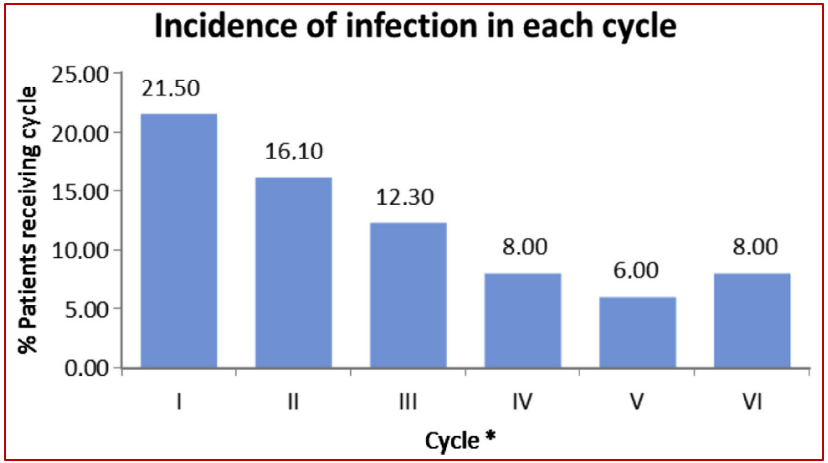


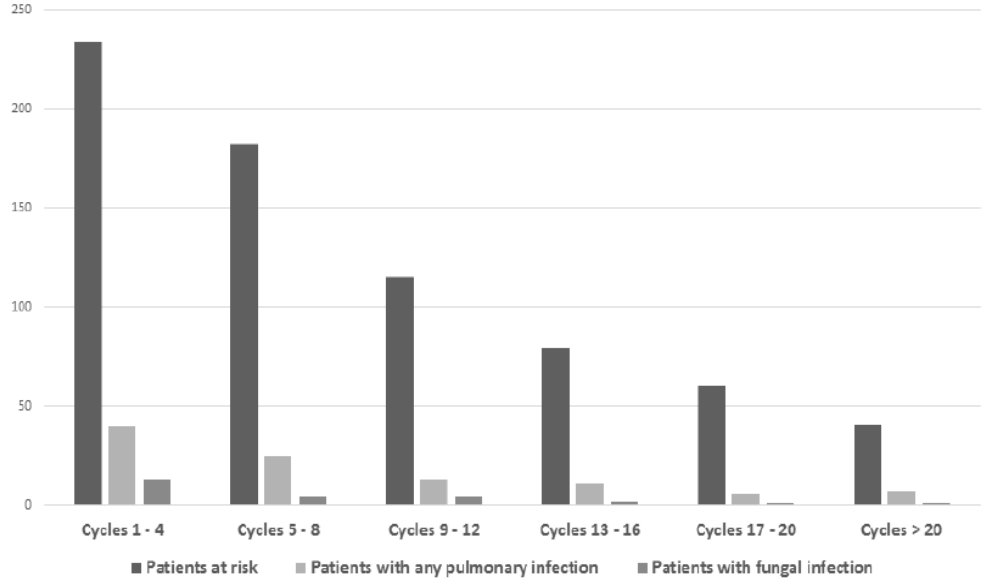
Table 4 Multivariate Analysis of Risk Factors for Infection and the Assigned Score

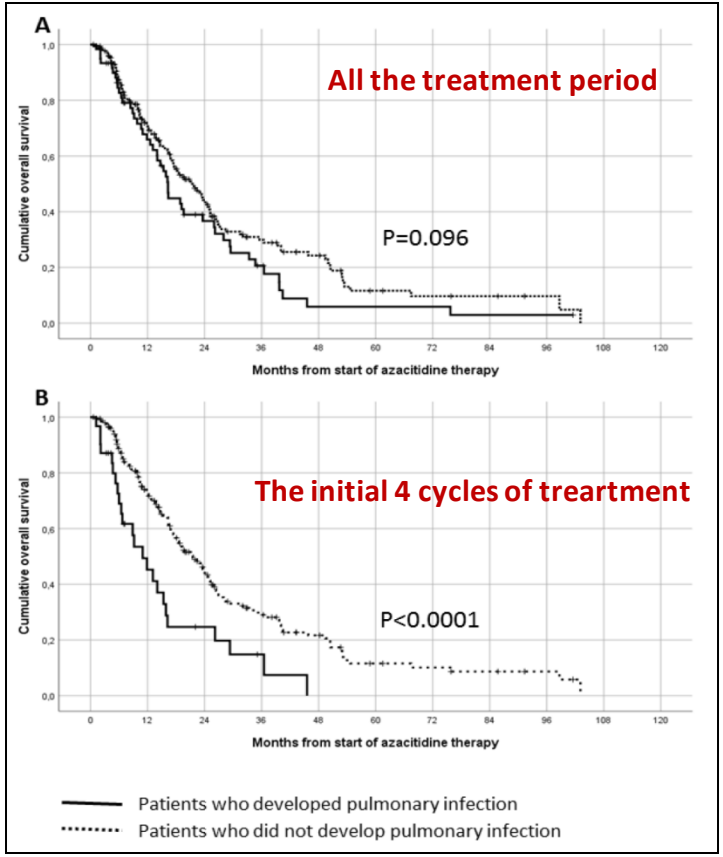
Parameter	Cutoff	Odds Ratio	97.5% Confidence Interval	*P*	Weighted Score
RBC Transfusion Dependency	Yes	2.38	1.21-4.79	.01	1
Neutrophil Count	$<0.8 \times 10^9$/L	3.03	1.66-5.55	<.01	1
Platelet Count	$<50 \times 10^9$/L	2.63	1.42-4.76	<.01	1
Serum Albumin	<35 g/dL	2.04	1.01-4.16	.05	1
ECOG	≥2	2.19	1.40-3.54	<.01	1

Pulmonary infections in MDS patients receiving front-line Aza

Latagliata R et al: Hematological Oncol. Epub 31.12.2019

- A continuous drop in frequency with the addition of new treatment cycles
- Major impact on survival the manifestation of pulmonary infection the initial 4 treatment cycles





Probability of death at 2 years following Aza treatment start

FACTOR	Odds Ratio (95% CI)	p
Age <70 vs ≥70 years	0.83 (0.62 – 1.21)	0.24
Underlying COPD	0.98 (0.60 – 1.13)	0.93
Underlying severe Diabetes	1.22 (0.67 – 2.20)	0.52
Hb levels <10 vs ≥10 g/dl	**1.89 (1.32 – 2.70)**	**<0.001**
Absolute PMN number <1.0 vs ≥1.0 x 10^9/L	**0.70 (0.57 – 0.95)**	**0.023**
Bone marrow blasts <10% vs ≥10%	**0.75 (0.58 – 0.96)**	**0.035**
Progression to AML	**2.16 (1.39 – 3.36)**	**<0.001**

Latagliata R et al: Hematological Oncol. Epub 31.12.2019

Sum up and Conclusions

- **Patient-related prognostic factors** should be evaluated **at baseline** and **at any time a therapeutic decision is taken in all patients with MDS**
- These include **comorbidity indexes, frailty and geriatric assessment and various Quality of Life tools**
- Useful and predictive patient-related prognostic tools are available, which **can be combined with the classical, disease-related prognostic systems**
- **Patient-related prognostic factors independently influence overall survival and non-leukemic death**
- **Patients with MDS have many predisposing factors for systemic infections, besides neutropenia**
- Systemic **infections are more commonly found during the initial cycles of treatment with HMAs** and are the major determinant of non-leukemic death

Thank you very much for your attention!