PATIENT GENERAL CONDITION AND THE OVERALL SURVIVAL OF OLDER ADULTS WITH MYELODYSPLASTIC SYNDROMES, AND RELATED DISEASES (CHRONIC MYELOMONOCYTIC LEUKEMIA AND ACUTE MYELOID LEUKEMIA)

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Introduction: Patient clinical situation at diagnosis (Dx) is a function of general condition *before Dx* and the impact of the new disease. ECOG performance status probably depends on both of them, and consequently may be highly dependent on the very moment that it is measured. General condition at baseline can be measured by Lee Index (LIx) for Older Adults[1] (see Table 1), a validated scale that has been shown to predict overall survival (OS) in a prospective and molecularly annotated cohort of Spanish Myelodysplastic Syndrome (MDS) patients.[2] To our knowledge, Lee Index has not been applied yet to MDS-related conditions, namely Chronic Myelononocytic Leukemia (CMML) and Acute Myeloid Leukemia (AML).

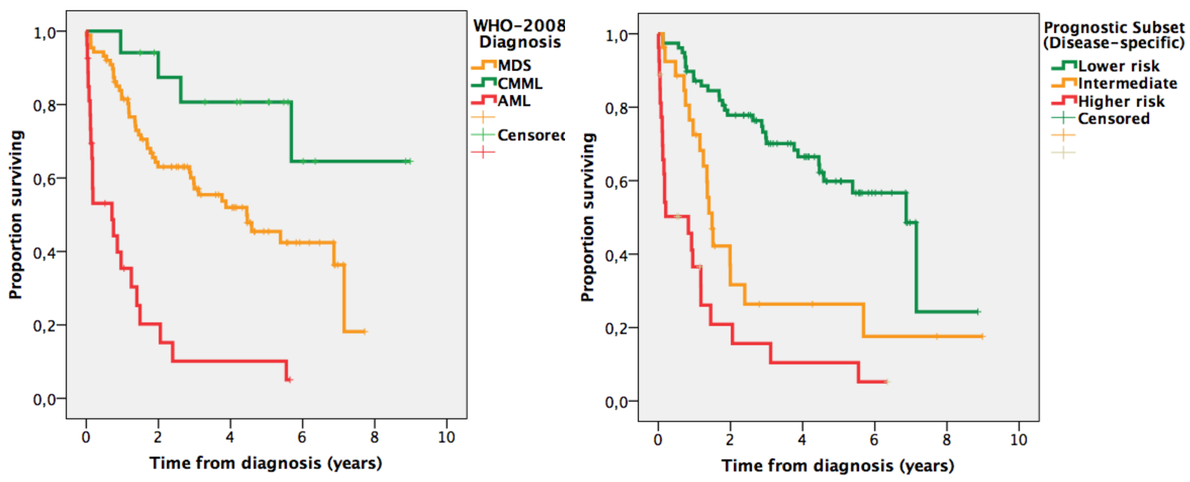
	Q1	Q2	Q3	Q4
Score	0-5	6-9	10-13	14+
4-year mortality				
Development cohort	3%	15%	40%	67%
Validation cohort	4%	15%	42%	64%

Table 1. Lee Index for Older Adults.[1]*Risk quartiles and 4-year predicted mortality*

Purpose: To analyze whether patient general condition before Dx is an independent determinant of OS in a heterogenous population of patients diagnosed with MDS and related diseases.

Methods: We have reviewed the clinical charts of 132 patients (84M, 48F), median age 79 years (IQR 73-82), diagnosed in our center with MDS (n=88), CMML (17) or AML (27), whose general condition had been evaluated by means of the Lee Index. The study was approved by our Institutional Review Board. All patients were diagnosed and classified according to WHO 2008 classification and stratified prognostically (Px) according to disease-specific criteria (MDS: IPSS-R[3], low-risk 65 patients, intermediate 11, high-risk 12; LMMC: CPSS[4]: low-risk 10, intermediate 5, high-risk 2; LMA: MRC/LRF[5], low-risk 3, intermediate 11, high-risk 13). ECOG was 0 in 23 patients (17.4%), 1-2 in 93 (70.4%), 3-4 in 15 (11.4%) and NA in 1 (0.75%). Twenty-two patients (16.7%) had received therapy known to prolong OS, while the rest had received only supportive care. After a median follow-up of 38.1 months (IQR 37.7-71.6), 70 patients (53.0%) had died, 45 (34.1%) were alive, and 17 (12.9%) were lost to follow-up. The proportion of them that received disease-modifying therapy was similar across the Dx and Px groups. OS was evaluated by Log-rank tests (for trend, as appropriate) and Cox regression models.

Results: OS was longest for CMML Pts (median NR), intermediate for MDS (53.4 months, IQR 29.1-77.7) and shortest for AML (8.5, IQR 0-19.1), p<0.001 (Log-rank). As expected, it was also progressively shorter as the disease-specific Px categories got worse (p<0.001, Log-rank for trend). ECOG categories were strongly associated with both LIx and Px categories (Chi-Square for trend 10.84, p=0.001 and 7.94, p=0.006, respectively), but not to the Dx category (p=0.55). LIx score ranged 0-19 points (median 8, IQR 6-10). Fifty-three Pts (40.2%) were included in the Q1 (score 0-5), 45 Pts (34.1%) in Q2 (6-9), 25 (18.9%) in Q3 (10-13) and 9 (6.8%) in Q4 (score 14+). As expected, LIx categories were associated neither with the Dx nor with the Px categories (p=0.15 and p=0.36, respectively). At first sight, we observed a non-significant univariate trend towards a shorter OS as the LIx got higher: Q1 68.2 months (IQR 25.6-110.9), Q2+Q3 45.2m (IQR 14.9-75.4) and Q4 16.2m (IQR 0-41.8); p=0.211 Log-rank) for trend). Interestingly, multivariate models disclosed that LIx score was an independent determinant of OS in this heterogeneous population, whether the type of treatment is included in the model or not (p= 0.019 and p=0.034, respectively).



	Wald	p-value
MODEL W/O TREATMENT		
Diagnostic group	15.46	p<0.001
Prognostic stratum	27.89	p<0.001
Lee index for older adults	4.47	p=0.034
MODEL WITH TREATMENT		
Diagnostic group	15.97	p<0.001
Prognostic stratum	24.58	p<0.001
Disease-modifying therapy	1.01	p=0.314
Lee index for older adults	5.49	p=0.019

Table 2. Multivariate analysis (Cox regression).
Disease-modifying therapy: Hematopoietic cell transplantation, intensive chemotherapy, hypomethylating agents

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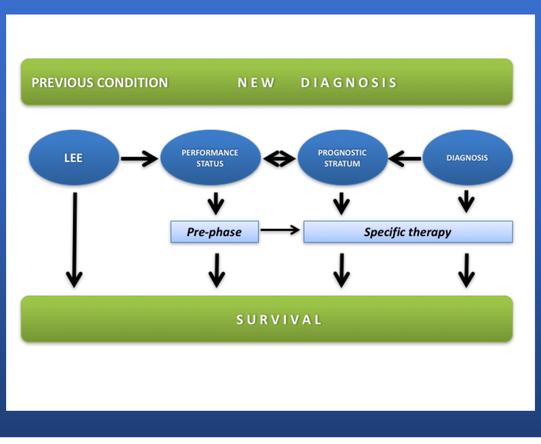
CONCLUSIONS:

Patient general condition, as evaluated multi-dimensionally by the Lee Index for Older Adults, is an independent determinant of OS in patients with MDS, CMML and AML.



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