Elevated IL-1β and Reduced IL-5 in Low-Risk Myelodysplastic Syndromes with Grade≥2 Bone Marrow Fibrosis

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INTRODUCTION

Myelodysplastic syndromes (MDS) are clonal hematopoietic cell disorders characterized by ineffective hematopoiesis, peripheral cytopenias and a risk of progression to acute myeloid leukemia. Diagnosis of myelodysplastic syndromes is based on morphologic assessment of dysplasia in the bone marrow aspirate. Routine trephine biopsy is not performed in all centers. As a matter of fact, bone marrow fibrosis (MF) is detected in both high and low risk (LR) MDS patients and, although relatively rare, is associated with dismal outcome and scarce response to standard therapy. Although MF may be associated with systemic inflammation and altered cytokine production, it remains unclear whether MF is a secondary event and whether the serum cytokine profile in fibrotic LR-MDS differs from that of non-fibrotic cases.

AIM

In this study we investigated the serum cytokine profiles in patients with LR-MDS evaluating their association with clinical features, outcomes and bone marrow fibrosis (MF).

METHODS

Clinical, pathological and laboratory data were collected and analyzed in a real-world single-center cohort of patients with LR-MDS.

- **Study population:** 87 patients with LR-MDS.
- **Bone marrow fibrosis:** Assessed on diagnostic bone marrow biopsy and classified as **MF0–1 (n=77)** or **MF≥2 (n=10)**.
- **Serum cytokine profiling:** Peripheral blood samples analyzed using the **ELLA multiplex immunoassay platform** (Bio-Techne).
- **Analytes (n=14):** IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-10, IL-13, IFN-γ, IFN-α, M-CSF, CCL3, CCL4, and MIG (CXCL9).
- **Statistical analysis:** Mann–Whitney U test (two-sided) for between-group comparisons; Kaplan–Meier analysis with the log-rank test for Overall Survival (OS) and Leukemia-Free Survival (LFS). No correction for multiple testing was applied; all *p*-values are reported as nominal.

RESULTS

Table 1: Bone marrow fibrosis assessment in patients in the FISiM Registry

Cases with informative biopsy (n = 4.304)	N (%)
MF0–1	3,829 (89%)
MF≥2	475 (11%)

Table 2: Patient characteristics in LR-MDS patients (Florence MDS Unit)

Clinical variables	MF0–1 (n=77)	MF≥2 (n=10)	p-value*
Age (years), median [range]	74.5 [43–87]	74.0 [48–85]	0.983
Sex, male, n (%)	54 (69%)	7 (70%)	1.000
Hemoglobin (g/dL), median [range]	10.6 [6.0–15.3]	9.1 [7.7–13.5]	0.308
Platelets (x10⁹/L), median [range]	132 [7–927]	204 [19–353]	0.455
IPSS-R score, median [range]	2.0 [1.0–4.5]	2.0 [1.0–2.5]	0.619
IPSS-M score, median [range]	−1.2 [−2.7 to 1.7]	−1.0 [−1.7 to −0.3]	0.365

- Overall 11% of cases enrolled in the FISiM registry presented MF≥2. We analyzed a small group of cases (87) from our center (Table 2).
- We did not confirm poorer outcomes (OS and LFS) in LR-MDS patients presenting MF≥2. No significant differences were observed between groups - log-rank test (Figure 1).
- **We analyzed 14 cytokines. Only 2/14 cytokines showed significant difference in serum levels in fibrotic vs non-fibrotic cases (Figure 2).**

CONCLUSION

LR-MDS patients with MF≥2 seem to display a cytokine pattern characterized by increased IL-1β and reduced IL-5, supporting inflammation-driven “reactive” fibrosis rather than a distinct biological MDS subtype. Our conclusions are preliminary due to the very limited number of cases

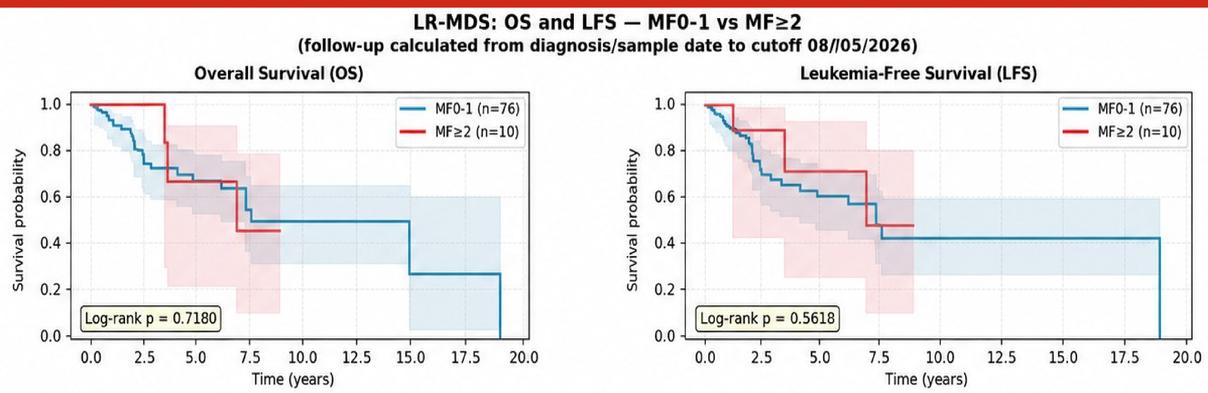

Figure 1. Overall Survival and Leukemia-Free Survival according to bone marrow fibrosis status.
Kaplan–Meier curves comparing **OS** and **LFS** in patients with **LR-MDS** stratified by bone MF (**MF0–1 vs MF≥2**). No significant differences were observed between groups (log-rank test).

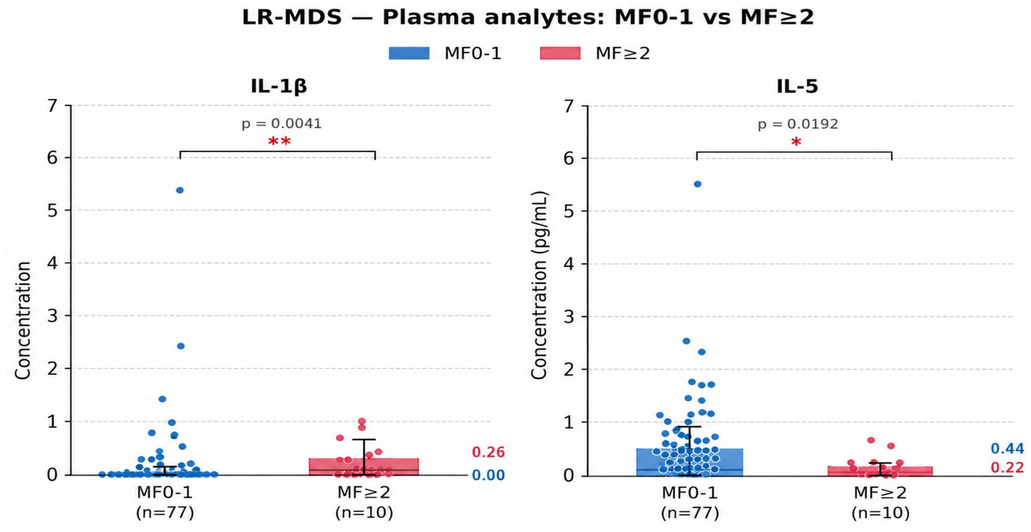

Figure 2. Differential expression of IL-1β and IL-5 according to bone marrow fibrosis.
Among the 14 analytes evaluated, only **IL-1β** and **IL-5** differed significantly between groups. **IL-1β** was increased in patients with **MF≥2**, whereas **IL-5** was higher in **MF0–1.**

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SOHO ANNUAL MEETING 2026