



Mutational landscape in patients with Myelodysplastic Syndromes, Experience in an Argentinian Center

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Background

Myelodysplastic syndromes (MDS) and chronic myelomonocytic leukemia (CMML) are heterogeneous myeloid malignant clonal disorders. Different mutations can be associated with higher risks of these diseases, specific characteristics, and responses to certain treatments. Molecular findings obtained through next-generation sequencing (NGS) have gained importance in myeloid neoplasms, but local access is limited. We recently incorporated NGS technology in our center that will seek to identify mutations.

Objective

To describe the mutational landscape of patients diagnosed with MDS and CMML locally.

Materials & Methods

We designed a prospective observational cohort study from July 2019 to July 2020 in adult patients diagnosed with MDS and CMML who underwent bone marrow biopsy with NGS at a private university reference hospital, Hospital Italiano, Buenos Aires.

Results

24 adult patients with MDS and CMML diagnosis were included. All patients were classified with IPSS-R. In table 1 patients characteristics. The mean Hb value in patients with 2 mutations or fewer was 10.3 mg/dl vs. 9.22 mg/dl in patients with ≥ 3 mutations ($p = 0.069$). Treatment was required in 50% of patients with 1–2 mutations and in 86% of patients with 3 mutations or more ($p = 0.016$). Five of six patients with CMML had a normal karyotype; all obtained at least three mutations, and SRF2 mutation was the most frequent. The most common mutational pathways involved in patients with adverse cytogenetics were DNA repair and transcription pathways ($p = 0.019$).

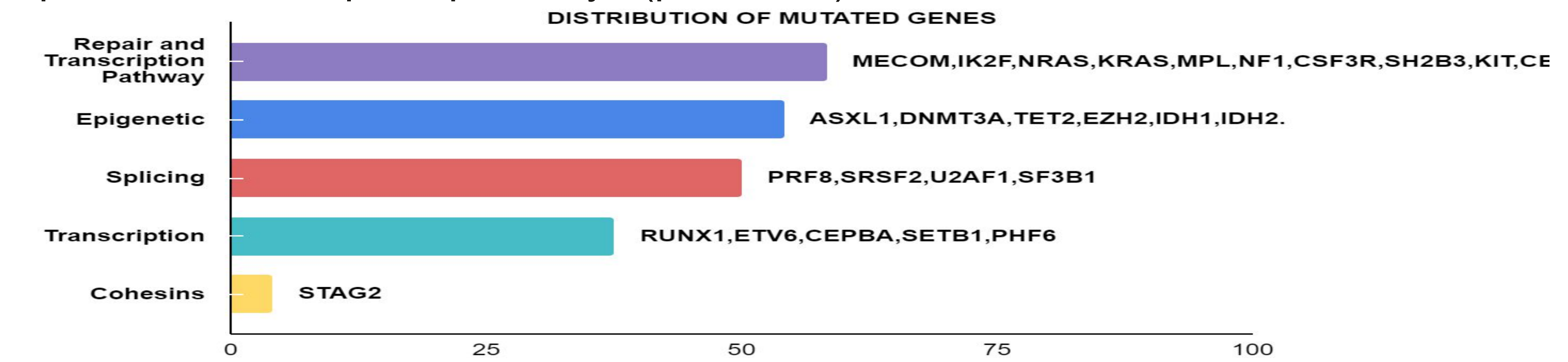
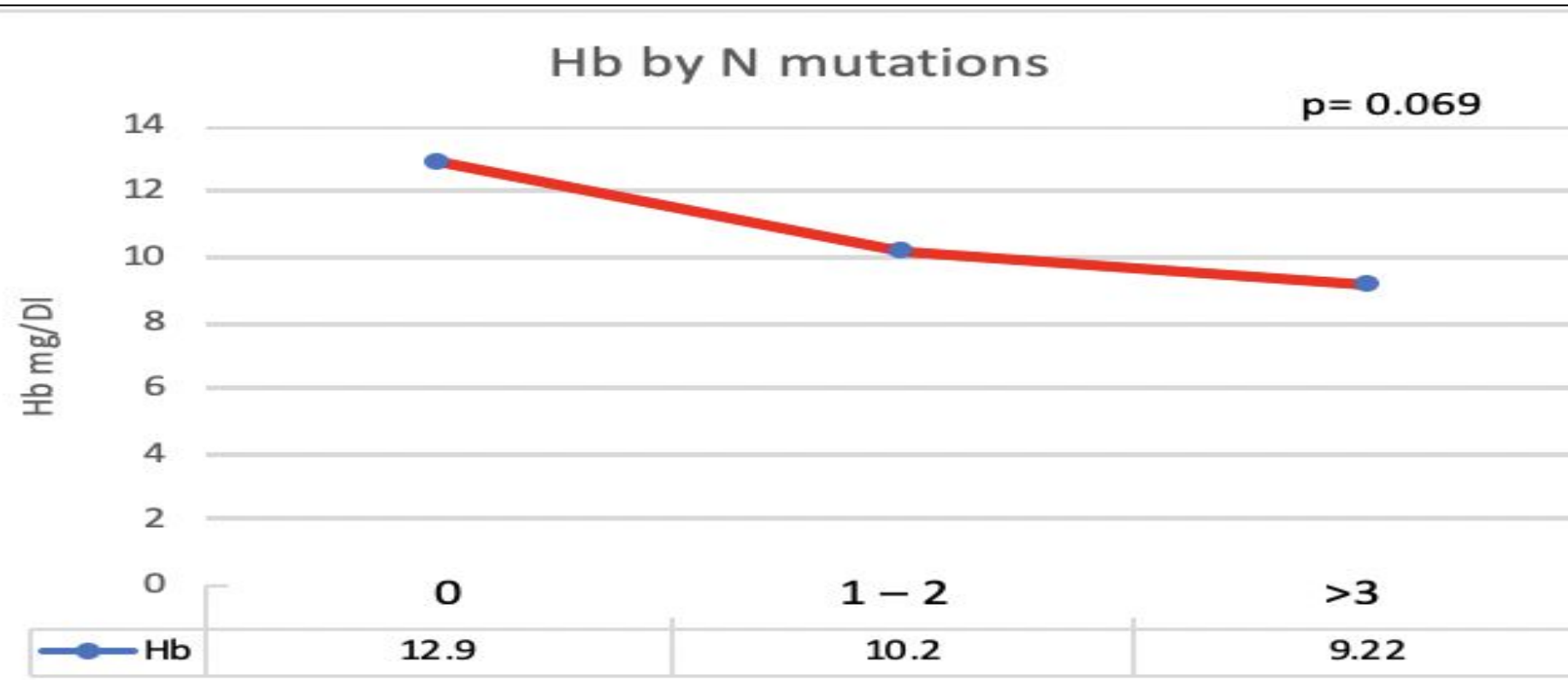


Table 1. patients characteristics.	N= 24	patients N (%) IPSS-R Low risk <3,5 IPSS-R High risk >3,5	15 (62.5) 9 (37.5)
LMMC N (%) SMD N (%)	18 (75) 6 (23)	Number of mutations low-risk IPSS R	2.2 (media)/1.7 S.D
Sex	Female 11 (45.8) Male 13 (54.2)	Number of mutations high-risk IPSS R	3.5(media)/1.8 S.D
Age median (IQR) years	74 Years (60-78,25 IQR)	MUTATION IN NGS N (%)	20 (86.9)



Discussion

The number of mutations was statistically correlated with the degree of anemia and with treatment indication. Recognizing mutations is crucial for clinical decisions, diagnosis, prognosis, and treatment. Although we have evaluated few patients, our data are comparable to those published and encourage us to continue working to improve the care of our patients.

References

- Such E, Francesc S. Grupo Español de Síndromes Mielodisplásicos (GESMD) guía de aplicación clínica de la secuenciación masiva en síndromes mielodisplásicos y leucemia mielomonocítica crónica 2017 pág 17-21
- Greenberg PL, Stone RM, Al-Kali A, et al. Myelodysplastic Syndromes, Version 2.2017, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2017;15(1):60-87.
- Gangat N, Mudireddy M, Lasho TL, et al. Mutations and prognosis in myelodysplastic syndromes: karyotype-adjusted analysis of targeted sequencing in 300 consecutive cases and development of a genetic risk model. Am J Hematol. 2018;93(5):691-697.
- Alfonso G, Arbelbide J, et al. Síndromes mielodisplásicos y síndromes de superposición mielodisplasia / neoplasia mieloproliferativa Sociedad Argentina de Hematología Guías de diagnóstico y tratamiento. pág 669-680.
- Hellström-Lindberg E, Tobiasson M, Greenberg P. Myelodysplastic syndromes: moving towards personalized management. Haematologica. 2020;105(7):1765-1779.