N-ras Mutation and its Prognostic Impact in Pediatric and Adult Patients with Myelodysplastic Syndrome treated with Allogeneic Hematopoietic Stem Cell Transplantation

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INTRODUCTION

The allogeneic hematopoietic stem cell transplantation (HSCT) is the only therapeutic option with a chance of cure for patients with myelodysplastic syndrome (MDS). Since MDS is a heterogeneous disease and allogeneic HSCT is a treatment that involves risks related to comorbidity and mortality, one of the most important aspects in the discussion is the criteria, the prognostic factors, used for its indication. Recently, some studies have analyzed the prognostic impact of some gene mutations in MDS patients treated with allogeneic HSCT, including the *N-ras* gene (Figure 1). A review of the literature showed that in Brazil there are still no studies reporting the evolution of patients with MDS after allogeneic HSCT and the presence of N-ras mutation. The aims of this study were analyse the frequency of N-ras mutation and its prognostic impact in pediatric and adult patients with MDS treated with allogeneic HSCT.

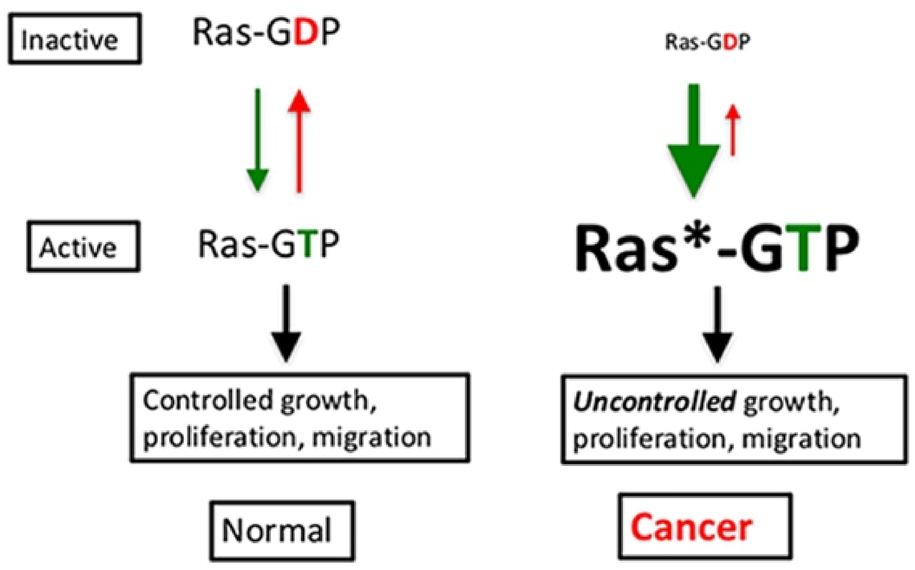
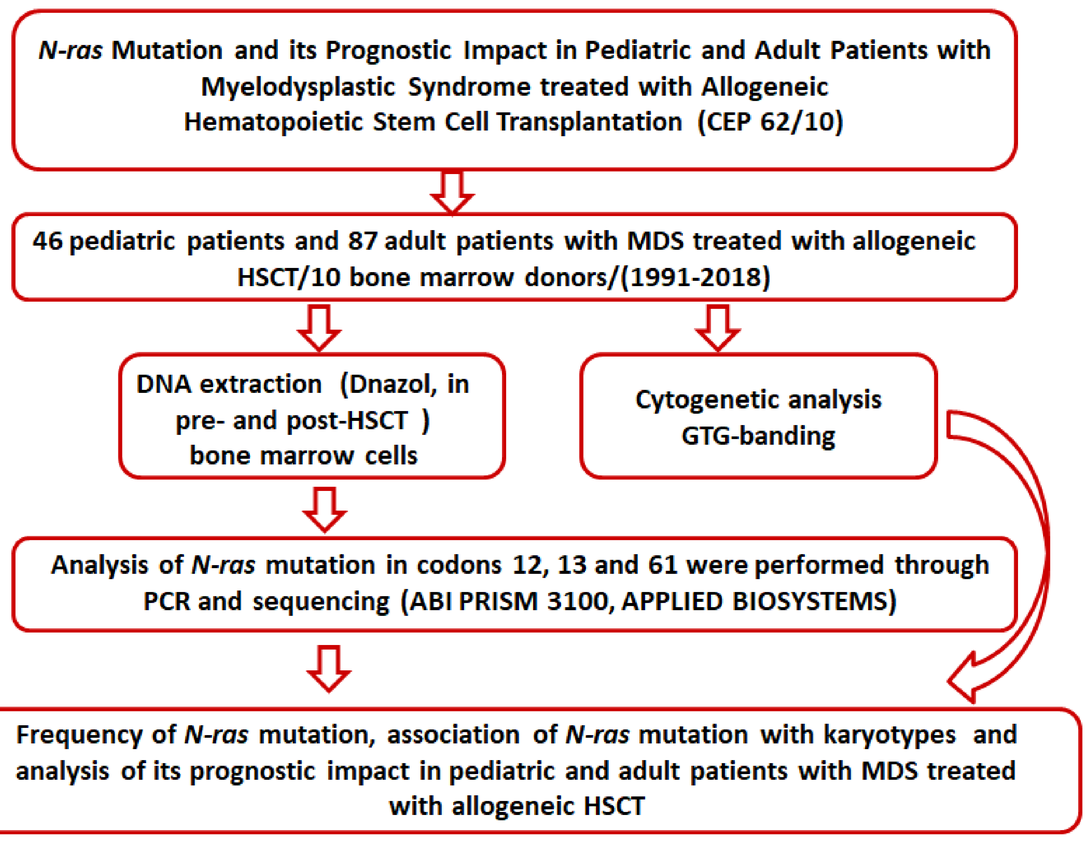


Figure 1: RAS proteins are important for normal development. Active RAS drives the growth, proliferation, and migration of cells. In normal cells RAS receives signals and obeys those signals to rapidly switch between the active (GTP) form and the inactive (GDP form) states. Mutated RAS* is stuck in the active state, ignores signals to the contrary, and drives cells to become cancerous. (Hartley J, NCI RAS Initiative, https://www.cancer.gov/research/key-initiatives/ras/about).

PATIENTS AND METHODS



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RESULTS

We observed the frequency of N-ras mutation in adult and pediatric patients in figure 2. The highest frequency of mutations occurred in the more advanced subtypes of the disease, both in pediatric patients and in adult patients (Table 2).

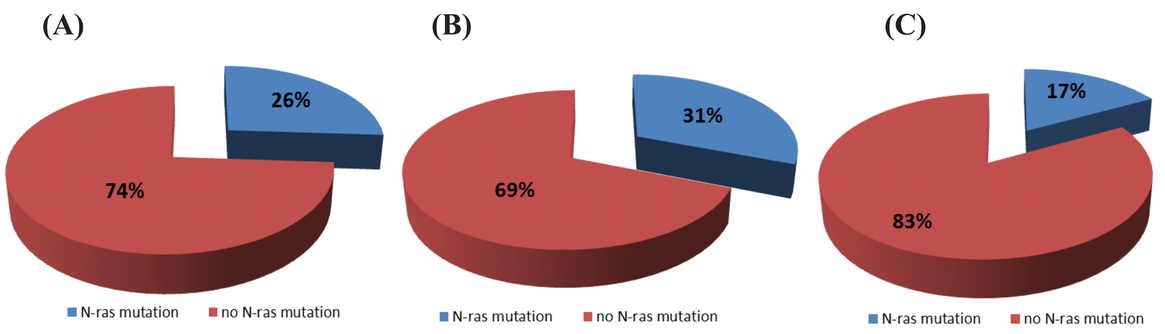

Figure 2: Frequency of *N-ras* mutation in patients with MDS before HSCT (A) Total of MDS patients; (B) adult MDS patients; (C) pediatric MDS patients.

Table 2: *N-ras* mutation in MDS subgroups

	Pediatric Patients		Adult Patients	
Subgroups	**Total of patients**	**Frequency of *N-ras* mutation (%)**	**Total of patients**	**Frequency of *N-ras* mutations (%)**
RC/RA	29	3 (10%)	56	10 (18%)
RAEB	11	3 (27%)	18	8 (44%)
RAEB-t	6	2 (33%)	13	9 (69%)
Total	46	8 (17%)	87	27 (31%)

The association with *N-ras* mutations with karyotypes of pediatric and adult patients showed that there is no specific chromosomal alteration associated with N-ras mutations. In initial MDS subgroup, mutations were observed in patients presenting normal karyotype and in abnormal karyotypes presenting: del(5q), del(12p), del(11q) and complex karyotype. In advanced MDS subgroups, mutations were observed in patients with normal karyotypes and abnormal karyotypes presenting: +8, del(11q)and complex karyotypes.

Of the 51 (38%) patients who presented relapse of the disease after allogeneic HSCT, 28 (55%) had N-ras mutated in pre-HSCT and post allogeneic HSCT (Figure 3).

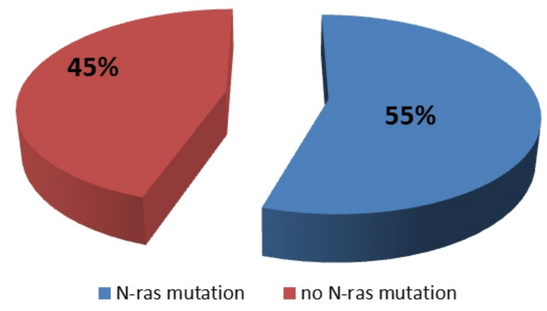

Figure 3: Frequency of *N-ras* mutation in patients with MDS who presented relapse of the disease after allogeneic HSCT.

CONCLUSION

Analyzing the mean time of disease relapse post-allogeneic HSCT, patients with *N-ras* mutation and chromosomal abnormalities presented an earlier relapse when compared to patients without mutations in the *N-ras* gene. Similar results were observed with *N-ras* mutation and normal karyotypes. The presence of *N-ras* mutation was an important marker in post-transplant, ading to understand the disease recurrence in patients with MDS presenting a normal karyotype.

Projeto Gráfico: Área de Edição e Produção de Materiais Técnico-Científicos / INCA

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