EXPLORING BIOINFORMATICS TOOLS FOR GRAFT-VERSUS-HOST DISEASE RISK PREDICTION IN HEMATOPOIETIC CELL TRANSPLANTATION

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HEMATOLOGÍA

AIM

To retrospectively analyze HLA-B locus dimorphisms and dissimilarities and their predictive significance in the development of acute graft-versus-host diseases (aGvHD) in patients undergoing haploidentical-related hematopoietic stem cell transplantation (HSCT).

METHOD

Retrospective study, data were collected from 87 patients who underwent haploidentical-related HSCT. Clinical information regarding aGvHD and high-resolution HLA typing (A, B, C, DRB1) of both donor and recipient were documented. The HLA-B Leader dimorphism was assessed utilizing the "HLA-B Leader Mismatch Calculator" by IPD-IMGT/HLA platform and the HLA-B Leader Assessment Tool (BLEAT). Additionally, the HLA-B dissimilarities algorithm was scrutinized using HistoCheck. Statistical analyses including Fisher's exact test, Tukey test, t-student test, and descriptive statistics were conducted using SPSS and Prism-GraphPad software, with significance set at $p<0.05$.

RESULTS

In the studied group (n=87), 57.5% were male and 42.5% were female, aged 1-79 years (mean: 24). Predominant diagnoses were acute lymphoblastic leukemia (32.2%), acute myeloblastic leukemia (29.9%), aplastic anemia (13.8%), Hodgkin's lymphoma 6.9%, myelodysplastic syndrome (5.7%), chronic myeloid leukemia (2.3%), and (9.2%) other hematologic neoplasms. HLA mismatches included 4/8 (78.2%), 3/8 (16.1%), 2/8 (3.4%), and 1/8 (2.3%). HLA-B Leader genotypes: identical (5.7%), MMM (4.6%), MMT (6.9%), MTM (6.9%), MTT (6.9%), TMM (4.6%), TMT (25.3%), TTM (9.2%), TTT (29.9%). TMT genotype showed the highest acute GvHD incidence (75.75%) with HLA-B Leader mismatch. Disparity scores in HLA-B didn't differ significantly between aGVHD responses. However, disparity scores were notably higher (24.49) in aGvHD with HLA-B Leader mismatch vs. those without (17.63) (p: 0.002, Tukey's test).

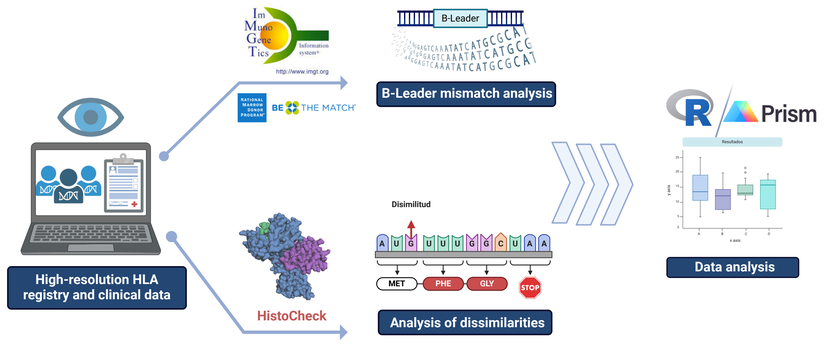

Figure 1. Methodology. High-resolution HLA typing of patients who received haploidentical-related transplants and their donors was recorded, in addition to their clinical history. B-Leader chain mismatch analysis and HLA-B dissimilarity algorithms were performed on the BLEAT IMGT IPD-IMGT/HLA and Histocheck platforms, respectively. Statistical analysis was performed with R and GraphPad Prism.

RESULTS

Dx

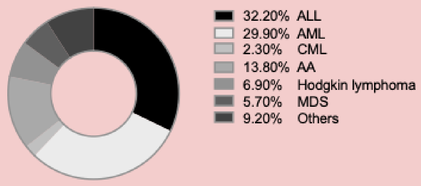

Figure 2. Diagnosis of the studied population.

HLA-B dissimilarity score, B-Leader mismatch and response to GvHD

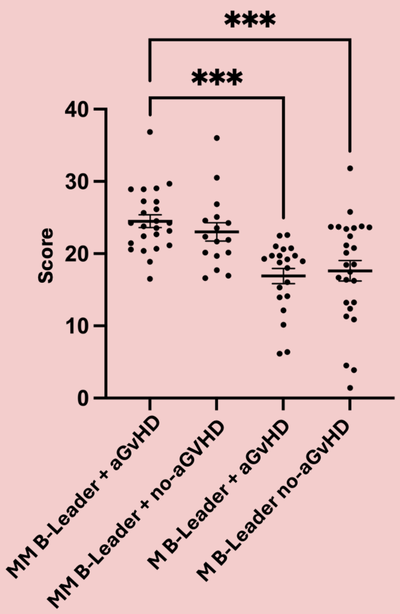

Figure 5. Dissimilarity score, B-leader mismatch and response to aGVHD.

Dissimilarity score

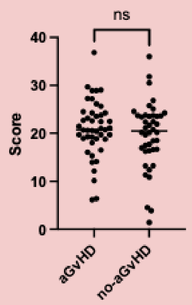

Figure 3. Dissimilarity score by HistoCheck.

B-Leader Genotypes

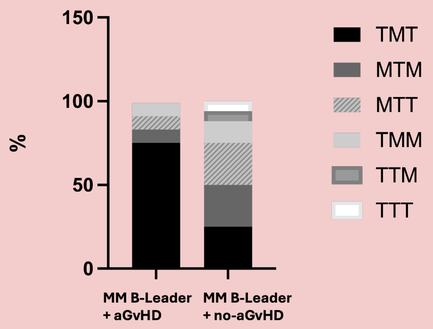

Figure 4. B-Leader genotypes.

In the studied population, 57.5% (50) were male and 42.5% (37) were female, with an average age of 24 years (range: 1-79 years). The most common diagnoses included acute lymphoblastic leukemia (32.2%, 28 cases), acute myeloblastic leukemia (29.9%, 26 cases), aplastic anemia (13.8%, 12 cases), Hodgkin lymphoma (6.9%, 6 cases), myelodysplastic syndrome (5.7%, 5 cases), chronic myeloid leukemia (2.3%, 2 cases), and other hematological neoplasms (9.2%, 8 cases), as shown in Fig. 2. The genotypes for the B-leader were as follows: identical (5.7%, 5 cases), MMM (4.6%, 4 cases), MMT (6.9%, 6 cases), MTM (6.9%, 6 cases), MTT (6.9%, 6 cases), TMM (4.6%, 4 cases), TMT (25.3%, 22 cases), TTM (9.2%, 8 cases), and TTT (29.9%, 26 cases) Fig. 4. The Fisher test revealed no significant relationship between the match/mismatch of the B-leader and the development of aGVHD on its ownm Fig. 3. However, the most frequently observed B-leader genotype associated with acute GVHD was TMT (75%) in cases of mismatch, Fig. 4. The dissimilarity score in HLA-B showed no significant differences when compared with the acute GVHD response. Nevertheless, the dissimilarity scores were significantly higher (24.49) in the group that developed acute GVHD with a mismatch in B-leader compared to the group that did not develop acute GVHD and had a match in the B-leader chain (17.63) ($p = 0.002$), as indicated by the Tukey multiple comparisons test Fig. 5.

CONCLUSION

The presence of the TMT genotype in HLA-B Leader dimorphism, coupled with a mismatch in the discordant HLA-B allele and a disparity score exceeding 18, elevates the likelihood of acute aGvHD onset in patients undergoing haploidentical-related HSCT. This criterion could be explored to improve donor selection and consequently the success of transplantation.