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To Remember the Importance of both Donor Choice and HLA Matching to Reduce Morbidity and Mortality after Allogeneic Hematopoietic Stem Cell Transplant (HSCT)

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Description

In this retrospective study concerning the Adolescent and Post-Adolescent (APA) patients, we have found several elements that were present in existing studies from the SFGM-TC register, in particular for risk factors of severe chronic and acute Graft-*versus*-Host Disease (GvHD) and the impact of HLA matching on Non-Relapse-Mortality (NRM) [1]. It was found that the use of Peripheral Blood Stem Cells (PBSC), the increasing donor's age and the receiver's age as risk factors of severe chronic GvHD. The use of Anti Thymocyte Globulins (ATG) or post-transplant cyclophosphamide was protective in this work as in various studies.

In a former study from the SFGM-TC register published in 2015, we studied the risk factors of sclerotic chronic GvHD in a cohort of 705 consecutive patients between 2005 and 2010 with the aim of confirming the risk factors (the use of Total Body Irradiation (TBI) and PBSC) that had been revealed in a large American study from Seattle [2,3]. The recipient's age and the use of PBSC were found as risk factors so the PBSC deleterious effect was confirmed. The patients were 3 to 70 years old with a median of 48 years old. Age was studied as a continuous variable and younger patients were shown to be at a greater level of risk. At this stage the age groups and the donor's age had not been unfortunately studied as a risk factor. The protective factors were the ATG use and cord blood as stem cells source which has been confirmed by many other studies.

Regarding the risk factors for severe acute GvHD (grade III and IV), we found in this APA patient's study: Active disease at transplant time and HLA matching (mismatch unrelated donor, matched unrelated donor and haplo-identical donor compared to sibling donor). The HLA matching had an important impact on NRM in addition the use of ATG was protective as for chronic GvHD [1].

As far as HLA matching is concerned, we conducted a retrospective study associating Swiss and SFGM-TC centers in a cohort of 251 patients between 2004 and 2010 in order to identify the impact of a mismatch on DRB3 or DRB4 locus after allogeneic HSCT with an HLA 10/10 matched unrelated donor [4]. In this study there was a significant impact of the DRB4 mismatch on overall survival, acute GvHD and transplant-related-mortality but an important limitation was that all DRB4 mismatches were associated with a least one DPB1 mismatch in this cohort. We found no impact of the DRB3 mismatch. This study was the starting point for studying the specific role of DRB3/4/5 mismatch independently from DPB1 mismatch in a large multicenter cohort of 2265 patients in France between 2000 and 2012 [5]. An important impact on GvHD and Relapse Free Survival (GRFS) and a high risk for acute GvHD (grade II to IV) but no impact on overall survival was revealed.

According to the available data from Easy match® in France, we know that among patients waiting for a matched unrelated donor, 35% to 40% have a high probability of obtaining 5 or more HLA 10/10 matched unrelated donors [6]. Easy match® is the software used by the French donor registry which was developed to help recipient centers in the search and identification of matched donors using haplotype frequencies to calculate the probability of phenotypic match in donors. Thus, it is relevant to select an unrelated donor matched for DRB3/4/5 and DPB1 when several HLA 10/10 matched donors are identified.

Conclusion

To conclude, it seems advisable to remember the importance of considering the donor's age, the HLA matching and the stem cell source associated with the type of transplant during the preparation phase of the procedure. This work should be completed in a multidisciplinary way, especially in association with the histocompatibility department, so as to reduce mortality and morbidity and improve the patient's quality of life after allogeneic HSCT.

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