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In the era of Transparent Reporting, how well do Hematopoietic Cell Transplant Centers Perform when they rely on Survival Analysis Scores to Attract Patients?

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Introduction

Hematopoietic stem cell transplantation (HSCT) stands as a well-established and widely embraced therapy for a spectrum of both malignant and non-malignant conditions. Varied perspectives and strategies regarding pediatric HSCT, distinct from those for adults, have been articulated by different groups, particularly concerning fundamental decisions and associated comorbidities. Despite these discussions, a comprehensive analysis focused specifically on pediatric-specific HSCT trends remains elusive.

Insights into transplant practices hold significant relevance for patients, donors, healthcare practitioners, and policymakers alike. Ultimately, such insights may contribute to forecasting future trends within the field and guide resource allocation to address patient needs effectively. This study outlines the landscape of pediatric HSCT for cancer cases in the United States spanning from 2008 to 2014, drawing upon data sourced from the Center for International Blood and Marrow Transplant Research (CIBMTR) [1].

Discussion

This pediatric-focused analysis from the CIBMTR illuminates current trends in the utilization of allo- and bus- HSCT for pediatric cancers in the United States. Mandatory reporting ensures that data captured by the Stem Cell Therapeutic Outcomes Database for allo-HSCT provides a comprehensive and reliable representation of current practices [2].

In the United States, unrelated donor transplants have surpassed transplants utilizing related donors for malignancies. The increase in unrelated donor transplants in the United States likely reflects an expanding unrelated donor registry, improved HLA matching, enhanced supportive care for HSCT, and similar considerations for related and matched unrelated donors. Additionally, the preference for bone marrow and umbilical cord blood grafts over peripheral blood stem cells for allo- HSCT in the pediatric setting has remained steady, likely due to the well-known increased risk of chronic GVHD associated with peripheral blood stem cell grafts [3]. Unrelated umbilical cord blood grafts are still utilized comparably with bone marrow grafts, which is likely attributed to the increased availability and improved quality of cord blood banks. However, it is possible that the use of unrelated umbilical cord blood grafts may decline in the future following the results of the Blood and Marrow Transplant Clinical Trials Network/Children's Oncology Group study, which did not demonstrate any survival advantage after a double umbilical cord blood transplant in hematologic malignancies, as well as with the increasing use of stem cell expansion modalities and haploidentical donor transplants. The overall cost of acquiring double cord units and considerations regarding improved stem cell doses in double cord blood units in individual cases may also continue to influence this trend [4].

Interestingly, within pediatric leukemia, total body irradiation (TBI) was utilized in 35% of acute myeloid leukemia (AML) cases, despite a lack of evidence supporting a distinct advantage of using TBI in children with AML in first complete remission or beyond. It is anticipated that the use of TBI in AML may decline in the future given emerging evidence demonstrating no superiority of TBI over busulfan-based regimens. Transplant trends for pediatric acute lymphoblastic leukemia (ALL) in second complete remission (CR2) and AML in first complete remission (CR1), the two most common indications, have remained unchanged over the last seven years [5]. However, it is acknowledged that ongoing clinical trials during the data collection period may have influenced several practices reported in this analysis. For example, the Bone Marrow Transplant Clinical Trials Network protocol 0501, a phase III, randomized, multi-institutional clinical trial comparing single versus double umbilical cord blood transplantation in children with hematologic malignancies using fludarabine, cyclophosphamide, and TBI as the conditioning regimen, may have impacted practices in this regard [6].

Furthermore, there was a notable increase in allo- HSCTs for Hodgkin lymphoma in 2011 followed by a gradual decline in subsequent years. This trend may be attributed to a retrospective report in 2010 demonstrating a survival advantage for patients undergoing reduced-intensity conditioning allo- HSCT for Hodgkin lymphoma after relapse following a prior autologous HSCT, which likely generated enthusiasm for this approach. However, it should be noted that the overall number of patients undergoing allo- HSCT for Hodgkin lymphoma remains relatively small, warranting cautious interpretation of this trend [7].

High-dose chemotherapy and autologous HSCT continue to be the standard of care for patients with Hodgkin lymphoma who relapse with no localized disease after frontline therapy, as evidenced by the increasing utilization of autologous HSCTs for Hodgkin lymphoma within the lymphoma group. Neuroblastoma remains the predominant indication for autologous HSCT over the past seven years. However, the recent decline in tandem transplants for neuroblastoma may be attributed to the increased use of targeted therapies such as anti-GD2 antibodies. It is important to evaluate this decline in future studies, particularly in light of recent randomized controlled trials demonstrating improved event-free survival with tandem transplants

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for neuroblastoma. Tandem transplants are also increasingly utilized for central nervous system tumors, consistent with data indicating improved survival with this approach. It is anticipated that this observed increase in tandem transplants for children with central nervous system tumors may evolve in the future with the initiation of the randomized clinical trial Head Start 4, which will randomize high-risk central nervous system tumor patients to receive either one or three busulfan-based transplants. Transplantation for Ewing sarcoma remains controversial, with conflicting reports regarding its efficacy [8].

Despite the large overall number of patients undergoing HSCT, several subcategories, including transplants for ALL in third complete remission (CR3), other unrelated donor transplants, and allo- HSCT for Hodgkin lymphoma, remain small. In conclusion, while most pediatric conditioning regimens in HSCT have remained stable over the last seven years, several important evolving trends have become apparent. There has been a recent decline in tandem transplants for neuroblastomas and an increase in tandem transplants for central nervous system tumors. It is presumed that tandem transplants for neuroblastoma may re-emerge in the future in the United States based on recent clinical trial results [9]. Additionally, tandem transplants may decrease for children with central nervous system tumors following the completion of Head Start 4, and the results of this trial may influence this trend in future studies. A slight decrease in ALL transplants in third complete remission is noted, likely attributed to improved prognostic factors and new cellular and targeted therapies that have emerged recently. The slight increase in the utilization of other unrelated donor transplants, despite relatively small numbers, warrants continued monitoring of this trend over time. Current publications addressing the increasing utilization of haploidentical transplants and declining use of double umbilical cord blood transplants are likely to further shape this landscape and should be closely examined in future reports. Additionally, further paradigm shifts in overall HSCT trends for cancer, particularly with the increasing use of cellular therapy and targeted immunotherapies for solid tumors, are anticipated [10].

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None

Conflict of interest

None

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