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OUTCOME & PROGNOSIS OF HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Abstract:

Introduction: *Hematopoietic stem cell transplant (HPSCT) specifically involves transplanting healthy stem cells from the bone marrow to the recipient with depleted bone marrow. If the donor and recipient are the same individuals, it's known as autologous and allogenic if they are different but of the same species. Donor cord blood is also sourced for this procedure. HPSCT can be used as bone marrow replacement therapy for certain extreme diseases, such as severe aplastic anemia, sickle cell disease, and cancers. This review will focus on its outcome and prognosis.*

Aim of the Study: *This review aims to discuss the outcome and prognosis of Hematopoietic stem cell transplantation.*

Methodology*: Comprehensive research of Hematopoietic stem cell transplant outcome and prognosis. The PUBMED search engine was the database used for the search process, with articles collected from 1957 to 2023. The term used in the search were: Hematopoietic stem cell transplant (HPSCT), outcome, prognosis, HLA typing, Engraftment, Conditioning*

Conclusion: *The hematopoietic stem cell transplant procedure is usually reserved for some instances of cancer and other extreme hematological diseases. The procedure carries a huge risk for complications which also can be fatal. There has been significant progress in the outcome and prognosis of HPSCT over the years, but much room remains for researchers and clinicians alike.*

Keywords*: Hematopoietic stem cell transplant (HPSCT), outcome, prognosis, HLA typing, Engraftment, Conditioning*

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INTRODUCTION:

Transplantation can be described as the transfer of tissue either in space, in time, or both. Hematopoietic stem cell transplant (HPSCT) specifically involves transplanting healthy stem cells from the bone marrow to the recipient with depleted bone marrow. If the donor and recipient are the same individuals, it's known as autologous and allogenic if they are different but of the same species. Donor cord blood is also sourced for this procedure. HPSCT can be used as bone marrow replacement therapy for certain extreme diseases, such as severe aplastic anemia, sickle cell disease, and cancers. This review will focus on its outcome and prognosis.

History

After a few experiments with mice, the first human trial of HPSCT was performed by Dr. Thomas in 1957, involving 6 cancer patients who were irradiated and placed on chemotherapy, and HPSC was transplanted from donors. The transplantation procedure was acutely successful in just 2/6 patients; all died by day 100. [1] No HLA matching was done in this trial as techniques weren't developed yet. Many years later, in 1977 and 1979, Thomas achieved 13% and 50% success, respectively. [2] Donor and recipient HLA matching was done in these trials, and HPSCT was performed earlier in the latter. Moreover, HLA matching from an unrelated donor dramatically increased the odds of matching. Fast forward half a century, and a million HPSCTs have been performed by 2012 with few acute mortalities. As of 2023, there are a staggering 40 million donors, according to the World marrow donor association. [3]

Types

HPSCT is usually indicated in hematological malignancies or severe anemias where the patient is irradiated and placed on chemotherapy to destroy bone marrow which feeds the malignancy. Such depleted bone marrow can then be transplanted by fresh hematopoietic stem cells as a replacement. Bone marrow depletion also helps avoid immune reactions against the grafted stem cells. [4]

Broadly HPSC can be sourced by three methods:

1. Autologous
2. Allogeneic
3. Umbilical cord blood

Allogenic HPSC can be further sourced from a related or unrelated donor. Related donors have a higher probability of HLA matching compared to unrelated donors, but related donors themselves are very limited in number. With advancements in HLA genotyping techniques and community efforts have created massive donor registries across the globe. [4]

Outcome

The ideal outcome of HPSCT is a complete disease-free state with little to no complications. However, HPSCT procedures are at constant risk of both acute and chronic complications, of which many of them are fatal. Acute and chronic infections are very common, especially in allogeneic transplantations. Graft rejection and graft-vs-host-diseases also appear due to HLA mismatching. Cardiovascular, nervous, and endocrine functions may also be compromised. Lastly, the risk of secondary malignancy remains high. [5]

Frietsch et al. 2022 retrospectively studied the outcome of 9299 allogenic HPSCT patients in Germany from 1998 to 2019. They found the median overall survival of 7.05 years with a 1/5/10-year survival probability of 0.70/0.53/0.47, respectively. Survival was better in the younger age group in the 2009-2019 time period, related to allogeneic donors and benign conditions. [6]

Factors influencing the outcome.

The outcome and prognosis of HPSCT can thus be dependent on a variety of factors such as age, performance status, underlying disease, conditioning methodologies, stem cell donor source used, level of HLA matching, engraftment parameters, and managing complications. [7]

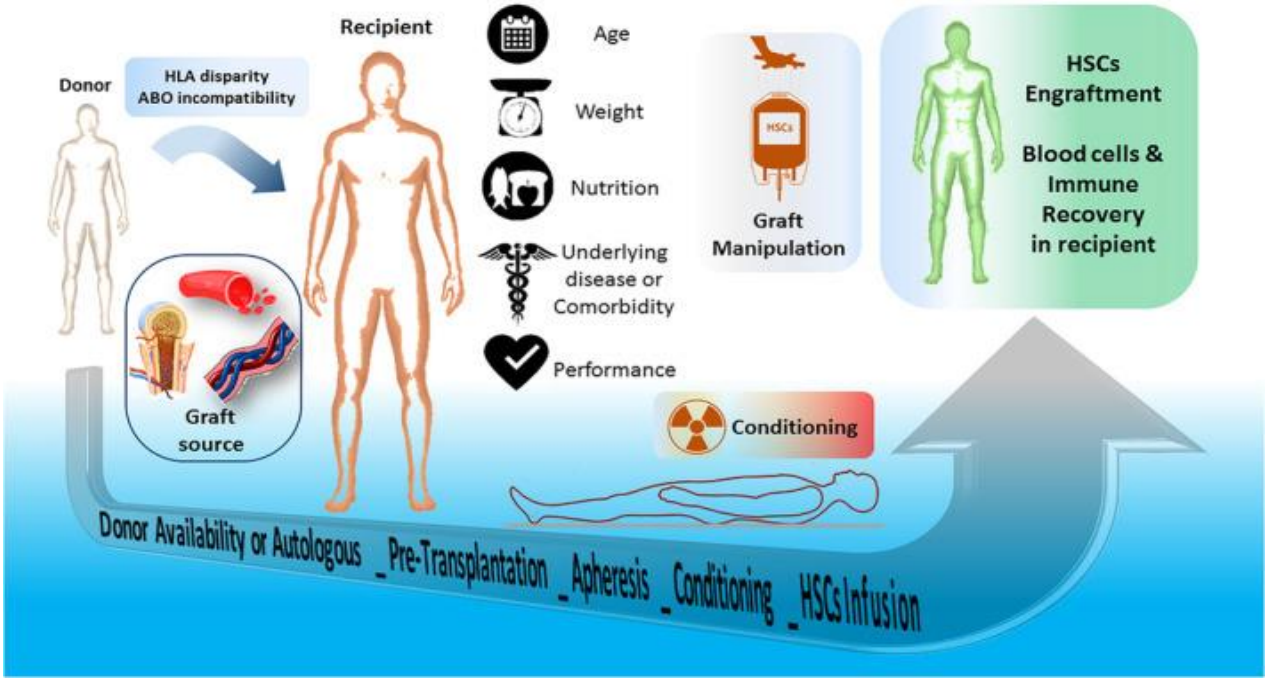

Image: Illustration describing factors affecting the outcome and prognosis of hematopoietic stem cell transplantation. [7]

HLA typing:

It is the most essential factor that determines the outcome and prognosis of HPSCT. Matched sibling donor is generally considered the first choice, which most recipients lack and must look for matched unrelated donor or cord blood. [8] Moreover, the degree of matching in the HLA genes is very sensitive to the outcome of HPSCT. Mayor et al. (2018) retrospectively studied 891 unrelated donors with allele-level resolution HLA matching in HPSCT. They retrospectively used next-generation gene sequencing technology to match the HLA genes with ultra-high resolution. This resulted in a change of matching status of around 29% of individuals and also showed improved overall survival among the remaining 71% of individuals compared to the newly discovered unmatched 29%. [9]

Conditioning:

The bone marrow niche must have its host hematopoietic cells and cancer cells destroyed before transplantation. This requires chemotherapeutic drugs such as busulfan and cyclophosphamide, which may predispose to morbidities if used more intensely. If used in lesser dosages, cytotoxic drugs may not kill native hematopoietic stem cells sufficiently, leading to host-vs-graft disease. More recently, researchers have been investigating the use of CD45 SAP (saporin), a CD45 antibody conjugated with a toxin that kills CD45-expressing nucleated cells such as lymphocytes and myeloid cells. These antibodies have also shown toxicity against in vitro leukemic cell lines. This targeted therapy may produce better clinical outcomes. **[10]**

Engraftment:

A sustained amount of hematopoiesis is the primary predictor of successful engraftment and a positive outcome. CD34+ cell count/kg infused and peripheral blood CD34+ count of greater than the median of 10 × 106/kg and 150 × 109/l positively influenced hematopoiesis and long-term peripheral blood counts. [11]

Comparison in Prognosis:

The procedure of HPSCT is indicated to select very extreme conditions where other therapeutic modalities have either failed or are likely to fail. They are mostly carried out on hematological malignancies with recurrences or a recurrence risk. Bornhäuser et al. 2023 performed a randomized clinical trial on 143 Acute myeloid leukemia patients where they split them into an HPSCT group and a standard consolidation chemotherapy group. Better disease-free survival and fewer relapse cases were observed in the HPSCT group. Higher non-relapse mortality was seen in the HPSCT group, which resulted in no significant difference in overall survival in both groups. [12]

Such comparisons of prognosis between types of HPSCT have also been studied with similar results. In a systematic review by Jun Du et al. (2021), a

Comparison of Allogeneic Stem Cell Transplant and Autologous Stem Cell Transplant in Refractory or Relapsed Peripheral T-Cell Lymphoma was made. More than 800 patients were evaluated in each group in terms of overall survival and progression-free survival. No significant difference in either of the survival was noticed. [13]

Chevallier et al. (2015) compared autologous vs. allogeneic umbilical cord blood stem cell transplants in patients with acute myeloid leukemia in second complete remission. Although the umbilical cord blood transplant group showed fewer incidences of disease relapse, it was accompanied by higher non-relapse mortality. The overall survival between the two groups was not significantly different. [14]

Cutler et (2006) studied 53 matched related donors and 30 unrelated donors in cases of hematological malignancies. They compared the incidences of graft-versus-host-disease, relapse-free survival, and overall survival in the two groups. No significant differences were found between the two groups. [15]

CONCLUSION:

The hematopoietic stem cell transplant procedure is usually reserved for certain cancer cases and other extreme hematological diseases. The procedure carries a huge risk for complications which also can be fatal. Certain factors play a significant role in determining its outcome and prognosis. There has been significant progress in the outcome and prognosis of HPSCT over the years, but much room remains for researchers and clinicians alike.

REFERENCES:

1. **Thomas E D, Lochte Jr H L, Lu W C, & Ferrebee J W (1957)**. Intravenous infusion of bone marrow in patients receiving radiation and chemotherapy. *New England Journal of Medicine*, *257*(11), 491-496.
2. **Thomas E D, Buckner C D, Clift R A, Fefer A, Johnson F L, Neiman P E, & Weiden P L (1979).** Marrow transplantation for acute nonlymphoblastic leukemia in first remission. *New England Journal of Medicine*, *301*(11), 597-599.
3. **Henig I, & Zuckerman T (2014).** Hematopoietic stem cell transplantation—50 years of evolution and future perspectives. *Rambam Maimonides medical journal*, *5*(4).
4. **Khaddour K, Hana C K, & Mewawalla P (2021).** Hematopoietic stem cell transplantation. In *StatPearls [internet]*. StatPearls Publishing.
5. **Hierlmeier S, Eyrich M, Wölfl M, Schlegel P G, & Wiegering V (2018).** Early and late complications following hematopoietic stem cell transplantation in pediatric patients–A retrospective analysis over 11 years. *PLoS One*, *13*(10), e0204914.
6. **Frietsch J J, Flossdorf S, Beck J F, Kröger N, Fleischhauer K, Dreger P, & Hilgendorf I (2023).** Outcomes after allogeneic haematopoietic stem cell transplantation in young adults in Germany. *British Journal of Haematology*, *201*(2), 308-318.
7. **Rafiee M, Abbasi M, Rafieemehr H, Mirzaeian A, Barzegar M, Amiri V, & Mohammadi M H (2021).** A concise review on factors influencing the hematopoietic stem cell transplantation main outcomes. *Health Science Reports*, *4*(2), e282.
8. **Kekre N, & Antin J H (2014).** Hematopoietic stem cell transplantation donor sources in the 21st century: choosing the ideal donor when a perfect match does not exist. *Blood, The Journal of the American Society of Hematology*, *124*(3), 334-343.
9. **Mayor N P, Hayhurst J D, Turner T R, Szydlo R M, Shaw B E, Bultitude W P, & Marsh S G (2019).** Recipients receiving better HLA-matched hematopoietic cell transplantation grafts, uncovered by a novel HLA typing method, have superior survival: a retrospective study. *Biology of Blood and Marrow Transplantation*, *25*(3), 443-450.
10. **Persaud S P, Cooper M L, Rettig M P, & DiPersio J F (2018).** Conditioning for hematopoietic stem cell transplantation using antibody-drug conjugate targeting CD45 permits engraftment across immunologic barriers. *Blood*, *132*, 2035.
11. **Duggan P R, Guo D, Luider J, Auer I, Klassen J, Chaudhry A, & Stewart D A (2000)**. Predictive factors for long-term engraftment of autologous blood stem cells. *Bone marrow transplantation*, *26*(12), 1299-1304.
12. **Bornhäuser M, Schliemann C, Schetelig J, Röllig C, Kramer M, Glass B, & Stelljes M (2023).** Allogeneic hematopoietic cell transplantation vs standard consolidation chemotherapy in patients with intermediate-risk acute myeloid leukemia: a randomized clinical trial. *JAMA oncology*, *9*(4), 519-526.
13. **Du J, Yu D, Han X, Zhu L, & Huang Z (2021)**. Comparison of allogeneic stem cell transplant and autologous stem cell transplant in refractory or relapsed peripheral T-cell lymphoma: a systematic review and meta-analysis. *JAMA Network Open*, *4*(5), e219807-e219807.
14. **Chevallier P, Labopin M, Socie G, Rubio M T, Blaise D, Vigouroux S, & Mohty M (2015).** Comparison of umbilical cord blood allogeneic

stem cell transplantation vs. auto-SCT for adult acute myeloid leukemia patients in second complete remission at transplant: a retrospective study on behalf of the SFGM-TC. *European journal of haematology*, *94*(5), 449-455.

15. **Cutler C, Li S, Ho V T, Koreth J, Alyea E, Soiffer R J, & Antin J H (2007).** Extended follow-up of methotrexate-free immunosuppression using sirolimus and tacrolimus in related and unrelated donor peripheral blood stem cell transplantation. *Blood*, *109*(7), 3108-3114.