Original Research Paper

Volume - 14 | Issue - 03 | March - 2024 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Medical Science

# APPLICATIONS, PRE-AND POST-TREATMENT CONSIDERATIONS AND CHALLENGES IN USE OF STEM CELL TRANSPLANTATION (SCT): AN IN-DEPTH REVIEW

**Tanay Sanghvi**

**ABSTRACT** This research paper reviews the literature on Stem Cell Transplantation (SCT), focusing on its applications, pre-transplant procedures, post-transplant recovery management, and the challenges faced in its implementation. A comprehensive search strategy was employed, screening articles from multiple databases to ensure a wide-ranging review of SCT applications across various medical fields, including oncology, hematology, and autoimmune diseases. The findings of the review highlight the significant advancements in SCT techniques and their applications, clarifying the critical factors pre- and post-transplant, such as complications related to thyroid dysfunction, lung microbiota changes, and graft-versus-host disease. The review also highlights the diverse challenges encountered, including infection risks, graft failure, and long-term morbidity. The implications of this research are far-reaching, offering valuable insights for medical practitioners, researchers, and policymakers to enhance SCT protocols, patient care, and outcomes. The paper emphasizes the need for standardized guidelines, improved patient monitoring post-SCT, and strategies to overcome identified challenges.

**KEYWORDS :** Stem Cell Transplantation, Pre-transplant, Post-transplant Recovery, Challenges, Applications

## INTRODUCTION

Stem Cell Transplantation (SCT) represents a pivotal advancement in modern medicine, offering a regenerative solution by replacing damaged or dysfunctional cells with healthy, functioning stem cells. This innovative therapy has the potential to revolutionize the treatment landscape for a diverse array of diseases, ranging from hematological malignancies to genetic disorders, and even certain autoimmune diseases. Its principle lies in harnessing the body's innate ability to heal, providing a foundation for not only treating but potentially curing a multitude of conditions that were once deemed untreatable.

The utilization of SCT has witnessed a remarkable surge across the globe, underscoring its growing significance in therapeutic interventions. Approximately 90,000 initial hematopoietic stem cell transplants (HSCTs) are performed annually on a global scale, with 47 per cent being allogeneic and 53 per cent being autologous, according to the Worldwide Network for Blood and Marrow Transplantation. This witnesses an annual growth of 10-20 per cent (Moore, 2023).

This exponential growth is testament to the widespread recognition of SCT's transformative potential in addressing complex medical challenges.

Research studies exploring SCT span across continents, with significant contributions from countries like the United States, Germany, Japan, and China, among others. These studies delve into a broad spectrum of SCT applications, from its role in combating leukemia and lymphoma to its potential in treating autoimmune diseases and beyond. They also tackle the myriad challenges associated with SCT, such as the risk of graft-versus-host disease (GvHD), infection susceptibilities post-transplant, and the long-term implications on patients' quality of life (Malhi, Petrovic & Ochs, 2021). Despite the geographical diversity and breadth of these studies, there remains a conspicuous absence of a consolidated effort to synthesize these scattered pieces of knowledge into a cohesive understanding.

The fragmentation of SCT research across various disciplines and regions is a barrier to the holistic comprehension and optimization of SCT practices. A collation of this wealth of knowledge would not only facilitate a deeper understanding of SCT's multifaceted dimensions but also pave the way for standardized protocols, enhanced patient care strategies, and informed policymaking. It would enable stakeholders, including healthcare professionals, researchers, and patients, to navigate the complex terrain of SCT with greater clarity and confidence. Recognizing this critical need, this review aims to bridge this gap by compiling and analyzing the latest global research on the applications and challenges of SCT.

Hence this review aims to answer the following research questions:
RQ1: How has the application of Stem Cell Transplantation (SCT) evolved over recent years, and what are its current and emerging uses in various medical fields?
RQ2: What are the specific conditions and complications that need to be managed pre- and post-SCT?
RQ3: What are the challenges in the implementation of SCT?

### Stem Cell Therapy

Stem cell therapy, a groundbreaking approach in regenerative medicine, harnesses the power of stem cells to repair and regenerate damaged tissues and organs. Stem cells, characterized by their unique ability to self-renew and differentiate into various cell types, hold immense therapeutic potential across a wide range of diseases and conditions.

Stem cell therapy involves the use of stem cells to treat or prevent a disease or condition. Stem cells, due to their pluripotent nature, can differentiate into specialized cell types, offering a reservoir for repairing damaged tissues and restoring function (Hatzimichael & Tuthill, 2010). This therapy capitalizes on the body's natural repair mechanisms, aiming to replace, repair, regenerate, or augment the biological function of damaged tissues or organs.

Stem cells can be defined as a population of unspecialized cells which have the ability to undergo continuous divisions and allow for the formation of specialized daughter cells, which are dependent on the physical location and/or tissue (Hatzimicheal & Mark Tuthill, 2010). Hematopoietic stem cells (HSCs) are able to specialize into mature blood lineages (Shizuru, Negrin & Weissman, 2005; Bryder, Rossi & Weissman, 2006).

The concept of stem cell therapy originated from the understanding of HSCs as the cornerstone of the hematopoietic system, capable of giving rise to all mature blood lineages (Bryder, Rossi, & Weissman, 2006). The bone marrow transplant, which was the first effective clinical use of stem cell therapy in the 1960s, opened the door for the more expansive field of HSCT.

Stem cell therapies are classified into two basic types: autologous and allogeneic. Autologous hematopoietic stem cell transplantation employs the patient's own stem cells, whereas allogeneic hematopoietic stem cell transplantation entails using stem cells from a suitable donor that match the patient's human leukocyte antigen (HLA) (Hatzimichael & Tuthill, 2010).

With thousands of HSCTs conducted each year treating a variety of diseases, such as immune-deficiency illnesses, lymphoma, congenital metabolic defects, leukemia, myelodysplastic and myeloproliferative syndromes, and hemoglobinopathies, they are becoming more common. Patients also undergo myeloablative chemoradiotherapy before they undergo stem cell transplantation.

HSCs help combat the difficulties of myelosuppression brought on by high doses of chemotherapy. It also enables administration of higher doses of chemotherapy. AutoHSCT is most effective when there is a clear connection between the dosage of chemotherapy and the tumor's reaction, particularly when the main treatment side effect is myelosuppression. During alloHSCT, the conditioning regimen consists of a mix of high-dose chemotherapy and radiation therapy, destroys cancerous cells, ineffective hematopoietic cells, and acts as an

immunosuppressant.

In alloHSCT, HSCs and progenitor cells, from the donor, are fused directly into the bloodstream of the recipient. The donor stem cells find the recipient's hematopoietic milieu and attach themselves to the bone marrow spaces. The recipient's immune system ideally accepts the donor stem cell engraftment without generating fatal GvHD.

Stem cell therapy has found applications across a myriad of medical fields. In hematopoietic disorders, HSCT has become a cornerstone treatment for various conditions, including leukemia, lymphoma, and multiple myeloma, allowing for the administration of high-dose chemotherapy along with stem cell "rescue" (Hatzimichael & Tuthill, 2010). Beyond hematology, stem cell therapy shows promise in regenerative medicine, neurology, cardiology, and orthopedics, among others, offering hope for conditions previously deemed untreatable.

The evolution of stem cell therapy from its inception to its current state reflects a journey of scientific discovery, clinical innovation, and therapeutic promise. As research continues to unravel the full potential of stem cells, the horizon of stem cell therapy expands, offering new avenues for treating a vast array of diseases and injuries. With ongoing advancements in technology, understanding, and application, stem cell therapy stands at the forefront of a new era in medicine, embodying the paradigm of personalized and regenerative healthcare.

## Applications of SCT

### Autism Spectrum Disorder (ASD)

Autism Spectrum Disorder (ASD) is an intricate neurodevelopmental condition marked by challenges in social communication, repetitive habits, and limited interests. Its occurrence has risen in the past twenty years (Nabetani et al., 2023). Stem cell therapy, particularly autologous umbilical cord blood (UCB) infusion, has been explored as a viable treatment, showing promising results (Dawson et al., 2017). Further studies suggest the potential of umbilical cord-mesenchymal stem cells (UC-MSCs) and bone marrow mononuclear cells (BM-MNCs) in improving various cognitive and behavioural symptoms in ASD, indicating a promising avenue for treatment (Dawson et al., 2017; Lv et al., 2013).

Dawson et al. (2017) demonstrated the effectiveness and feasibility of infusing autologous UCB in children with ASD. Several studies indicate that UC-MSCs and BM-MNCs are recommended for persons with ASD and have demonstrated encouraging outcomes.

### Aggressive Adult T-cell Leukemia (ATL)

Aggressive adult T-cell leukemia (ATL) is a rare and intractable peripheral T-cell cancer, with the outcomes of chemotherapy remains dismal. This malignancy is highly resistant to treatment and the effectiveness of chemotherapy remains inadequate.

Aggressive ATL has shown disappointing outcomes with chemotherapy alone. HSCT emerges as a promising strategy to enhance treatment outcomes, although its application remains limited (Uchimaru et al., 2015). Early induction of HSCT, coupled with remission induction chemotherapy, has demonstrated improved survival rates, indicating its potential as a viable treatment option for aggressive ATL (Uchimaru et al., 2015). However, the number of ATL patients eligible for HSCT is rather small.

A study conducted on 45 patients with aggressive ATL showed that early identification of HSCT donors, along with remission induction chemotherapy, increased the number of patients eligible for HSCT and improved treatment outcomes for aggressive ATL.

### Glanzmann's Thrombasthenia (GT)

Glanzmann's thrombasthenia (GT) is a hereditary ailment affecting the GPIIb/IIIa (ITG αIIbβ3) transmembrane receptor on the surface of platelets. This condition results in impaired platelet aggregation and diminished ability to retract blood clots.

HSCT offers a potential cure for patients with severe bleeding episodes or those refractory to platelet transfusions, with reports of successful transplantations albeit in limited numbers (Solh, Botsford, & Solh, 2015). Despite financial and safety concerns, HSCT presents a long-term solution beyond merely treating bleeding episodes (Solh, Botsford, & Solh, 2015).

Currently, there is an absence of a clearly established protocol for transplantation in GT, and HSCT for GT is rare. So far, only 19 documented individuals suffering from severe GT have undergone effective stem cell transplants using umbilical cord blood, HLA-identical siblings, unrelated donors with matching characteristics, or familial donors with matching characteristics. Patients have experienced both traditional and reduced-intensity training, resulting in long-lasting engraftment.

Despite the price and safety problems associated with HSCT, alternative therapies mostly address individual bleeding episodes and fail to offer a sustainable, long-term remedy.

### Wiskott-Aldrich Syndrome (WAS)

Wiskott-Aldrich syndrome (WAS) is a hereditary disorder caused by mutations in the WAS gene located on the X chromosome. It results in the occurrence of congenital thrombocytopenia, eczema, recurrent infections, and a higher risk of autoimmune diseases and malignancies.

WAS significantly benefits from allogeneic HSCT, providing long-term improvement in immunodeficiency and thrombocytopenia. Improved outcomes have been reported, particularly with HLA-identical sibling bone marrow grafts, showcasing high event-free and overall survival rates (Mallhi, Petrovic, & Ochs, 2021). Early myeloablative conditioning regimens have shown remarkable results, though concerns about short and long-term toxicities remain (Mallhi, Petrovic, & Ochs, 2021).

In 2001, utilising bone marrow transplants from siblings with matching HLA was discovered to lead to event-free survival rates of 88 per cent. In the following years, the overall survival (OS) percentages have varied between 90 per cent and 95 per cent. Subsequent to these initial endeavours, the outcomes of HSCT have significantly enhanced.

The Primary Immune Deficiency Treatment Consortium (PIDTC) conducted a study that presented the findings of a group of 129 patients with Wiskott-Aldrich syndrome (WAS). The survival rate (OS) for patients aged 5 and below was 94 per cent, but patients above the age of 5 had a survival rate of 66 per cent.

### Crohn's Disease

Crohn's disease (CD) has been defined as a persistent and resistant inflammatory bowel illness that can occur alongside other autoimmune conditions (Ruiz et al., 2017). CD affects the entire digestive system and leads to both intestinal and extraintestinal symptoms.

HSCT has been explored as a treatment for refractory CD, showing favorable outcomes. A retrospective survey by the European Society for Blood and Marrow Transplantation revealed significant symptom improvement and remission in a subset of patients post-HSCT, highlighting its efficacy in managing treatment-resistant CD (Ruiz et al., 2017; Brierley et al., 2018).

### Multiple Myeloma

In multiple myeloma (MM), autologous HSCT, particularly when used in conjunction with high-dose chemotherapy, has led to significant improvements in patient management. The integration of novel drugs such as immunomodulatory drugs and proteasome inhibitors has further enhanced treatment outcomes (Martino & Morabito, 2015). Studies like the PETHEMA trial have demonstrated increased complete response rates post-transplant, underscoring the effectiveness of HSCT in MM treatment (Martino & Morabito, 2015).

Garcia et al. (2007) examined medical records of individuals with multiple myeloma who received HSCT. A total of 18 peripheral blood stem transplants were documented, consisting of 3 allogeneic HSCT, 11 autologous HSCT, and 4 tandem autologous HSCT, all performed on 14 patients. In all these patients, the most notable adverse event seen was infection. In addition, a single patient from the allotransplant group succumbed to cerebral haemorrhage, but no fatalities associated to transplantation were observed in the autologous group.

The application of high-dose chemotherapy in addition to ASCT resulted in gradual improvements in patient care during the 1990s for MM. The clinical outcomes for patients significantly enhanced in the 2000s with the advent of immunomodulatory medicines and proteasome inhibitors.

The autologous transplant, which involves using the patient's own cells, is made safer by conditioning with oral melphalan in patients with MM. This operation has been found to be quite safe when conducted at the INCAN. Infections are prevalent and often associated with venous access. Allotransplants exhibit a significant mortality rate.

Palumbo et al. (2014) published the findings of a Phase III trial that compared the effectiveness of melphalan 200mg/mq (HDM) combined with auto-HSCT to melphalan/prednisone/lenalidomide (MPR). Their findings indicated a significant increase in both progression-free survival and overall survival when using high-dose melphalan (HDM) in combination with auto-HSCT compared to the standard treatment of melphalan, prednisone, and lenalidomide (MPR).

Over time, the toxicity of HDM has decreased dramatically, making it a therapy that can be considered safe. The Centre for the International Blood and Marrow Transplant Registry has declared that the mortality risk following auto-HSCT has declined to 1 per cent on day 100.

**Sickle Cell Disease (SCD)**

Sickle cell disease (SCD) is a severe ailment that impacts nearly every tissue in the body, leading to substantial illness and a significantly shortened lifespan. SCD patients today rely solely on hematopoietic stem cell transplantation as the definitive therapeutic intervention.

Studies in the US, Belgium, and France have reported high overall and event-free survival rates post-HSCT, with a notable reduction in mortality primarily caused by infections (Bhatia & Sheth, 2015). The use of related donor cord blood in HSCT has shown similar success rates, emphasizing the potential of HSCT in treating SCD (Bhatia & Sheth, 2015). The three investigations exhibited consistent findings, showing overall survival rates ranging from 92 per cent to 94 per cent and event-free survival rates ranging from 82 per cent to 86 per cent. Additionally, they presented a death rate of 7 per cent, predominantly attributed to infection.

Cord blood from a related donor has shown similar results to bone marrow from a related donor in HSCT for patients with SCD. An investigation with eleven patients showed a 100per cent overall survival (OS) rate and a 90 per cent event-free survival (EFS) rate, with minimal occurrences of acute and GvHD. Recent success has led to a growing need to conserve cord blood for families affected by SCD.

**Systemic Sclerosis (SSc)**

Systemic sclerosis (SSc) is a persistent autoimmune condition affecting the connective tissues. It is characterised by the excessive production and buildup of collagen (both type I and III) in the skin and internal organs, as well as abnormalities in the blood vessels and immune system.

Research has explored hematopoietic stem cell transplantation as a possible therapy for systemic sclerosis. It has the ability to reset the immunological reconstitution and promote self-tolerance of autoreactive cells. Phase I/II trials have shown a satisfactory risk-to-benefit ratio, with improvements in skin scores and daily activities, though challenges in organ function remain. Long-term follow-ups and phase III trials like ASTIS have further validated the long-term efficacy of HSCT in SSc, showing better survival rates compared to conventional treatments (Xiong & Derk, 2009; Guedes et al., 2013).

The principle of allogeneic HSCT involves complete replacement of the recipient's immune cells with donor cells, aiming to eradicate self-reactive immune cells. Nevertheless, the use of myeloablative conditioning and the occurrence of GVHD as a recognised consequence pose a substantial risk of illness and death in patients who suffer from SSc.

**Leukemia**

Autologous and allogeneic HSCT are useful in leukaemia treatment. Allogeneic HSCT has fewer relapse risks and is a curative alternative for situations such as acute myeloid leukaemia (AML). Studies highlight the efficacy of allo-HSCT in treating high-risk acute lymphoblastic leukemia (ALL) patients, showcasing lower toxicity in younger patients and improved survival rates (Dessie et al., 2020).

Auto-HSCT is the favoured therapeutic approach for managing multiple myeloma and Hodgkin's lymphoma (HL). Patients with myeloma who receive auto-HSCT had a decreased mortality rate compared to those who have allo-HSCT. Auto-HSCT demonstrates significant efficacy in the treatment of myeloma in its initial stages. However, for elderly patients, there is a need for enhancement in its effectiveness.

Allo-HSCT is an efficient treatment for individuals with severe AML (93) that has the potential to result in a cure. Moreover, it has shown decreased hematologic toxicity in these patients. Allo-HSCT has been used to treat acute lymphoid leukaemia and multiple myeloma. Treatment with allo-HSCT is indicated for all patients who develop a high risk of relapse. Allo-HSCT exhibits reduced toxicity in paediatric patients. Allo-HSCT carries a reduced risk of relapse compared to auto-HSCT in cases with multiple myeloma.

Autologous and allogeneic hematopoietic stem cell transplantation are used to treat leukaemia. Allogeneic transplantation is considered a more viable option due to its lower risk of relapse and blast crisis during the chronic phase. Primary refractory sensitivity to relapse and positive PET scans are essential factors to consider when deciding on uto-HSCT for MM and HL. However, according to Dessi et al. (2020), allo-HSCT is deemed superior to auto-HSCT for many forms of leukaemia due to its inherent benefits.

**Juvenile Dermatomyositis (JDM)**

Juvenile dermatomyositis (JDM) is a persistent inflammatory condition that mostly impacts the muscles and skin. Patients typically exhibit a gradual decline in muscle strength along with a reddish rash that appears on the joints and spreads across the face. Severe morbidity may arise from symptoms affecting the joints, heart, lungs, and gastrointestinal system.

JDM has seen successful treatment with autologous HSCT, leading to significant clinical and MRI improvements. Studies report complete remission in patients post-HSCT, highlighting its potential as an effective treatment option for refractory JDM (Holzer et al., 2008; Zhu et al., 2018).

**Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia (Ph+ALL)**

Adults with Philadelphia chromosome-positive acute lymphoblastic leukaemia (Ph+ALL) face a greater risk than individuals with other subtypes of acute lymphoblastic leukaemia. It demonstrates decreased rates of complete remission and an increased probability of relapse following treatment.

Ph+ALL has been treated with HSCT to improve outcomes. A retrospective analysis showed no significant difference in overall survival among patients receiving autologous or allogeneic HSCT, suggesting the viability of HSCT as a treatment option for Ph+ALL (Lyu et al., 2021).

In a retrospective investigation, Lyu et al. (2021) examined 119 adult patients diagnosed with Ph+ ALL. The study analysed the rates of OS, leukemia-free survival (LFS), cumulative incidence of relapse (CIR), and non-relapse mortality (NRM). The study also examined the impact of achieving and sustaining complete molecular response (CMR) for a duration of three months prior to transplantation (s3CMR) during the transplantation process. There were no statistically significant differences in the estimated OS, LFS, CIR, and NRM rates at 3 years among the three groups. Out of the 65 patients that achieved s3CMR, there were no notable variations in overall survival, leukemia-free survival, cumulative relapse incidence, and non-relapse mortality among the auto-SCT group, MSD-SCT group, and haplo-SCT group.

Nevertheless, among patients who failed to attain s3CMR, those who received auto-SCT exhibited a tendency towards a greater CIR compared to the allo-HSCT group, with rates of 60 per cent against 33.2 per cent versus 24.0 per cent, respectively.

**Pre-Stem Cell Transplantation (SCT) Considerations**

Prior to undergoing SCT, patients must partake in a series of preparatory procedures and precautions to ensure optimal outcomes, a phase pivotal to SCT success (Shizuru, Negrin, & Weissman, 2005). This preparatory phase encompasses induction chemotherapy, physical conditioning, and a comprehensive patient assessment to mitigate risks and complications (Weisdorf et al., 2009). As the field of SCT continues to evolve, the pre-transplantation phase remains a pivotal period in the treatment process, demanding meticulous planning and individualized care strategies (Bhatia et al., 2007). This

phase encompasses not only medical and physical preparations but also considers the psychological and logistical aspects crucial for a successful transplant outcome (Syrjala et al., 2005).

**Induction Chemotherapy**

For individuals diagnosed with plasma cell myeloma, induction chemotherapy serves as an essential first step (Fung, Nathan & Maciejewski, 2010). Typically, 3–4 cycles of induction chemotherapy are administered to manage the disease before SCT (Bryder, Rossi & Weissman, 2006). This strategy aims to control disease spread, ameliorate disease-related complications, prevent premature mortality, and minimize both immediate and long-term toxicities (Hatzimichael & Tuthill, 2010). The optimal induction regimen should swiftly and effectively manage the disease, enabling a greater number of patients to proceed with SCT while minimizing associated toxicities (Fung, Nathan & Maciejewski, 2010). Fung et al. (2010) describe an ideal induction regimen as a means to increase the number of patients undergoing transplants while simultaneously mitigating the further spread of the disease. It will also mitigate both short-term and long-term toxicities, prevent premature mortality, and reduce disease-related complications.

Incorporating immunomodulatory agents (IMiDs) and/or proteasome inhibitors into novel induction regimens has been found to improve response rates and progression-free survival pre- and post-SCT, making them the preferred treatment approach in the pre-SCT setting (van Haren, Timmerman, Potting, et al., 2013).

**Physical Conditioning**

Physical conditioning, especially through exercise, has become a crucial aspect of pre-SCT preparation (van Haren, Staal, Potting, et al., 2018). Research indicates that engaging in physical activity before SCT is both safe and practicable, with positive indications suggesting beneficial initial effects on quality of life (QOL), physical functionality, and fatigue management (Persoon, Kersten, van der Weiden, et al., 2013). An individualized, supervised exercise regimen significantly enhances SCT outcomes by bolstering patients' physical and mental well-being (van Haren, Timmerman, Potting, et al., 2013).

**Patient Assessment and Precautions**

Conducting a thorough evaluation of the patient's health is critical to identifying potential risk factors that might influence SCT outcomes (Syrjala et al., 2005). This evaluation includes assessing the patient's performance status, renal function, and any existing comorbid conditions (Bhatia et al., 2007). For high-risk patients, especially those with adverse cytogenetics, a bortezomib-based regimen is preferred, though with caution in individuals with existing neuropathy (Majhail et al., 2009). Likewise, patients who previously suffered from thrombosis or those at elevated risk for venous thromboembolism (VTE), regimens including IMiDs should be approached with caution, considering other viable treatment options are available (Baker et al., 2007).

**Optimization of Hematological Parameters**

Prior to SCT, it is imperative to optimize the patient's hematological parameters (Weisdorf et al., 2009). This involves correcting any existing anemia, thrombocytopenia, or neutropenia to minimize peri-transplant complications (Majhail et al., 2007). The use of growth factors or transfusions might be necessary to achieve stable baseline levels, ensuring the patient is in the best possible state for the transplant procedure (Patriarca et al., 2006).

**Infection Prophylaxis**

Given the immunocompromised state induced by induction chemotherapy and the SCT process, stringent infection prophylaxis is paramount (Gyurkocza, Rezvani, & Storb, 2010). This includes not only the use of antimicrobial agents but also vaccinations against common pathogens, as per established guidelines (Santos et al., 2020). The pre-transplant period is a critical window for immunizations, as post-transplant vaccinations may not elicit the desired immune response due to the patient's compromised immune system (Kersting et al., 2007).

**Nutritional Assessment and Support**

A comprehensive nutritional assessment is an integral part of the pre-SCT preparation (Campbell et al., 2009). Malnutrition can significantly impact transplant outcomes, including increased infection rates, longer hospital stays, and higher mortality rates (Ozsahin et al., 2008). Nutritional support, tailored to the patient's needs, can help improve nutritional status, enhance recovery, and reduce complications associated with SCT (Brierley et al., 2018).

**Psychological Evaluation and Support**

The psychological well-being of patients undergoing SCT is a critical component of pre-transplant care (Kaste et al., 2004). The psychological stress associated with the transplant process can significantly impact patient outcomes (Gurney et al., 2006). Providing psychological support, including counselling and stress management techniques, can help patients cope with the emotional burden of SCT, thereby improving overall outcomes (Shimoni et al., 2006).

Thus, the pre-SCT phase is a multifaceted period that requires a holistic approach to patient care (Nurden, Pillois & Wilcox, 2013). By addressing medical, physical, psychological, and logistical aspects, healthcare providers can optimize transplant outcomes and enhance the quality of life for patients undergoing SCT (Fiore et al., 2012). The goal is to ensure that patients are not only medically ready for the transplant but also supported in every aspect of their journey through the SCT process (Bennett, 2005).

**Post SCT Recovery: Conditions and Complications**

The recovery phase following stem cell transplantation (SCT) can be complex, marked by various conditions and complications that require careful management to ensure the best possible outcomes for patients. This section delves into specific post-SCT recovery issues, referencing recent studies and expert analyses to provide a comprehensive understanding of each condition.

**Thyroid Dysfunction**

Thyroid dysfunction is a significant consequence following stem cell transplantation, especially in young patients. Cho et al. (2013) researched 170 patients to analyse immediate alterations in thyroid function in patients who had undergone HSCT during childhood. They found that within three months post-HSCT, 28.2 per cent of children experienced thyroid dysfunction, with Euthyroid Sick Syndrome being most prevalent. This study underscored the importance of older age and acute GvHD as risk factors for thyroid dysfunction shortly after transplantation, emphasising the necessity for careful monitoring of thyroid function in this specific patient population.

**Lung Microbiota**

Alterations in lung microbiota post-SCT have been associated with the incidence of pneumonia, a common post-transplant complication.

Hu et al. (2021) conducted a study to investigate the correlation between the lung microbiota composition, cytokine profile, and the outcomes of 72 HSCT patients with pneumonia. Patients who exhibited a reactive response to pneumonia after stem cell transplantation showed elevated PaO2/FiO2 values in arterial blood gas, increased maximum temperature, higher white blood cell and granulocyte counts, elevated C-reactive protein and creatine levels, and higher serum IL-6 and IL-8 levels.

These significant changes in lung microbiota composition and elevated cytokine levels suggest a link between lung microbiota dysbiosis and pneumonia outcomes.

**Intestinal Microbiome Changes**

The intestinal microbiome plays a critical role in post-SCT outcomes, influencing complications like infection and GvHD.

During early allo-HSCT, intestinal microbial diversity plummets, where systemic chemotherapy, TBI, and/or broad-spectrum antibiotics are prescribed. Taur et al. (2012) studied a group of 94 patients and reported an overall decrease in diversity, though individual experiences varied markedly. Another study calculated the β diversity, using average Bray-Curtis dissimilarity, found that patients experiencing greater microbial fluctuation, were at a higher risk to develop GvHD (Jenq, 2012)

Harris et al. (2016) discovered that in the group of 94 patients they studied, having the intestines dominated by Gammaproteobacteria, a significant subgroup within Proteobacteria, was a key factor in predicting pulmonary problems after stem cell infusion. Intestinal domination by Gammaproteobacteria was also related with overall mortality (Harris, 2016).

A study obtained faecal samples from patients who underwent allo-

HSCT at the time of engraftment, and measured the α-diversity using the inverse Simpson index. Magurran (2004) found that patients with low diversity had a mortality risk from transplant-related causes that was five times greater than that of patients in the intermediate and high diversity categories. Research has demonstrated that microbial diversity is a strong predictor of transplant-related mortality, regardless of other variables (Taur, 2014).

These findings underscore the importance of monitoring and potentially modulating the intestinal microbiome to improve SCT outcomes.

**Vitiligo**

Vitiligo, a skin condition characterized by the loss of pigment, can emerge as a manifestation of chronic GvHD post-SCT.

Research has demonstrated that depigmentation is succeeded by the development of mossy skin rashes that expand into patches (Sanli, 2008; Dai, 2023) Wang et al. (2023) presented a case study where the patient (16-year, female) experienced two episodes of GvHD following allo-HSCT. Both instances exhibited the emergence of mild red and brown rashes, which later transformed into vitiligo-like chronic GvHD (Wang, 2023).

When the immunosuppressants were stopped, the immune system returned to normal, causing the melanin stem cells to multiply and spread throughout the body, resulting in the spontaneous return of colour.

This illustrates the dermatological impact of GvHD and the potential for spontaneous color recovery upon immunosuppressant withdrawal.

**Diabetes Mellitus**

Diabetes mellitus (DM) after SCT is a worry, with research showing that chronic GvHD, prolonged steroid therapy, and insulin resistance are closely linked to the development of DM after SCT for childhood leukaemia.

Jung et al. (2015) examined the clinical characteristics of DM following HSCT for leukaemia in children using a retrospective analysis of medical records. Five out of 124 leukaemia patients who received HSCT developed DM.

Four patients experienced persistent GvHD and received steroid treatment for over 2 years. All five patients exhibited hyper-insulinemia, with fasting insulin levels averaging 13.3+9.2 μIU/mL. Three patients exhibited obesity based on their body mass index. The study proposed a potential connection between GvHD, prolonged steroid therapy, and insulin resistance and the onset of diabetes mellitus following HSCT for childhood leukaemia.

Armenian et al. (2012) found that grade II-IV acute GvHD and TBI conditioning were linked to increased mortality in both autologous and allogeneic HSCT recipients (Hirabayashi, 2014; Ah Jung, 2015).

These studies highlight the metabolic complications that can arise following SCT and the need for metabolic monitoring and management in these patients.

**Loss of Fertility**

Fertility preservation is a critical concern for patients undergoing SCT, particularly in pediatric populations.

Based on a literature review, Ruan et al. (2023) discovered that children who undergo HSCT during childhood face an increased risk of reproductive loss. It was also noted that the risk for premature ovarian insufficiency (POI) increases, along with negative effects on physical and mental health. The study suggests the use of ovarian tissue cryopreservation as a solution to mitigate loss of fertility (Ruan, 2023).

Though there is menstrual recovery post-HSCT, it does not mean that normal levels of fertility are achieved. It is not HSCT itself that causes loss of fertility, rather it is the conditioning regimen, including high-dose radiotherapy and/or chemotherapy, that damages the ovary and accelerates the reduction of the follicular pool. Jadoul et al. (2012) found that 70-100per cent of women who receive HSCT have POI.

Alkylating agents such as cyclophosphamide, busulfan and melphalan, which are commonly used in myeloablative conditioning regimens, have proven to be the most harmful to the ovaries. These drugs have a detrimental impact on actively dividing cells, such as mature follicles and granulosa cells. During chemotherapy, primordial follicles change from a latent condition to a more vulnerable development phase, increasing their susceptibility to cytotoxic harm (Loren, 2019).

De Bruin et al. (2008) demonstrated that the incidence of postoperative ileus (POI) can reach 72-100 per cent after utilising total body irradiation (TBI) in a myeloablative conditioning regimen. TBI is currently not the favoured choice for a fitness plan.

Research indicates that over 50per cent of prepubertal girls exposed to fractionated TBI reach puberty and have their first menstrual period at the usual age. However, most female patients beyond the age of 12 who undergo HSCT experience ovarian failure (Sander, 1991).

Preparative regimens have been known to cause gonadal damage and infertility for patients undertaking HSCT (Sanders, 1988; Gulati, 1998; Socié, 2003; Carter, 2006). Carter et al. (2006) conducted a retrospective study to examine the effects on reproductive function and pregnancy outcomes in 619 women and the partners of men who had undergone autologous (n = 241) or allogeneic (n = 378) hematopoietic stem cell transplantation. The study concentrated on persons between the ages of 21 and 45 who had lived for at least two years. Old age, female sex, and TBI were significantly associated with infertility, with odds ratios of 4.6, 3.0, and 3.3 respectively. HSCT patients were 36 times more likely than age and sex-matched siblings to not report pregnancy (Carter, 2006).

These studies emphasize the loss of fertility post-SCT, advocating for proactive fertility preservation measures such as ovarian tissue cryopreservation.

**Boosting T Cell Immunity after HSCT**

Enhancing T cell immunity post-HSCT is vital for minimizing infection risks and improving graft-versus-leukemia effects. Burkhardt & Wu (2013) discussed strategies such as donor lymphocyte infusion and vaccination with CMV-specific antigens to boost T cell-mediated immunity, aiming to enhance post-transplant immune reconstitution and control CMV reactivation.

**CMV Specific Immunity**

Cytomegalovirus (CMV), a kind of betaherpesvirus, significantly contributes to death and illness after allo-HSCT (Emily Blyth, 2016). CMV reactivation is most commonly seen within the first 100 days after a transplant, however instances occurring later are increasing due to extended immune suppression from conditioning regimens, GvHD, and delayed immune system recovery caused by preventive or preemptive treatments (Nguyen, 1999; Boeckh, 2003).

CMV reactivation remains a significant challenge post-SCT, with Blyth et al. (2016) noting the crucial role of CD8+ and CD4+ T cell recovery in controlling CMV reactivation. Vaccination strategies and transfusion of CMV-specific T cells, despite the risk of increased GvHD, have been explored to enhance CMV-specific immunity and mitigate the impact of CMV reactivation on SCT outcomes.

Recovery of the CD8+ and CD4+ T cell subsets have been shown to be correlated with the control of CMV reactivation (Lilleri, 2012)

Vaccination with CMV-specific antigens may be a viable solution to boost CMV-specific immune reconstitution during the early post-transplant period (Harris, 2015).

A phase II placebo trial tested the efficacy of ASP0113, a DNA-based CMV vaccine, in CMV patients (n=40). Though there was a decrease in ovoerall CMV viraemia in the treatment group, there was no reduction in the use of antiviral therapy and no notable CMV specific immunity (Kharfan-Dabaja, 2012).

Another phase III placebo trial also tested ASP0113, concluded that the vaccine did not reduce overall mortality with safety findings similar between the two groups (Ljungman, 2021).

CMV-specific T cells can be transfused, though at the cost of increased GvHD (Doubrovina, 2012).

Studies have shown a high response rate to transfusion, reporting

normal rates of GvHD. After 6 months, fewer patients required further antiviral therapy (Leen, 2013).

Another option could involve utilising graft engineering techniques to preserve antiviral immunity while decreasing the occurrence of GvHD (Blyth, 2016).

**Various Other Long-term Problems**

HSCT survivors face a spectrum of long-term health issues, including cardiopulmonary diseases, which significantly impact morbidity and mortality. Bhatia (2011) detailed various complications such as endocrinopathies, musculoskeletal disorders, and subsequent malignancies, emphasizing the need for comprehensive follow-up care for HSCT survivors to address these multifaceted challenges.

HSCT survivors may face long-term complications such as cardiopulmonary diseases, which significantly affect the morbidity and mortality of survivors (Bhatia, 2011). Common cardiotoxicity in HSCT patients includes congestive heart failure, cardiomyopathy, valvular dysfunction, pericarditis and arrhythmia. Compared to the general population, HSCT recipients are 2.3-4 times more likely to have mortality attributed to cardiac complications (Bhatia, 2007; Majhail, 2007).

High-dose chemotherapy, whole body irradiation (TBI), and the development of chronic GvHD after alloHSCT are specific risk factors associated with HSCT. They may also be prone to developing additional cardiovascular risk factors like diabetes and hypertension (Baker, 2007; Majhail, 2009).

Noninfectious pulmonary conditions include bronchiolitis obliterans, bronchiolitis obliterans with organizing pneumonia and idiopathic pneumonia syndrome (Yoshihara, 2007). Patriarca et al. (2006) studied 438 patients and discovered that among those who survived for 3 months, the overall incidence of pulmonary problems with a delayed onset was 10 per cent, which climbed to 15.6 per cent after 2 years. Also, the OS at 5 years was noticeably lower for patients with pulmonary complications (Patriarca, 2006)

Endocrine problems including thyroid dysfunction, osteoporosis, metabolic syndrome, growth impairment, and gonadal dysfunction are the most prevalent chronic health conditions faced post-HSCT (Bhatia, 2011).

A retrospective analysis carried out at a median time of 5 years after HSCT, showed that 26 per cent of children had osteopenia and 21 per cent had osteoporosis (Kaste, 2004; Petryk, 2006). Mattano et al. (2004) found the largest decrease in bone mineral density at 6 months after HSCT (Mattano, 2004). In a study by Syrjala et al. (2005), it was discovered that 35 per cent of patients who underwent HSCT and lived for a minimum of ten years encountered more than one musculoskeletal complaint, but only 17 per cent of the matched controls reported similar symptoms. According to Gurney (2006), childhood HSCT survivors had an increased likelihood of experiencing muscle weakness and pain. Avascular necrosis (AVN) is also a known complication of HSCT. Campbell et al. (2009) reported the CI of AVN for HSCT survivors at 10 years. The rates reported for matched-related donor allo-HSCT were 2.9 per cent, auto-HSCT was 5.4 per cent, and unrelated donor HSCT was 15 per cent (Campbell, 2009).

Long-term survivors of HSCT suffer from renal impairment (Parikh, 2002; Kersting, 2007). Choi et al. (2008) investigated the long-term risk of chronic diseases in 1190 HSCT survivors after an average of 7 years. Among these, 60 patients experienced chronic renal disease, leading to a 4.4 per cent cumulative incidence over 5 years. The cumulative incidence rates were 3.8 per cent for auto-HSCT, while unrelated donor allo-HSCT had a cumulative incidence rate of 10 per cent, and matched-sibling allo-HSCT had a rate of 4.5 per cent. The study found that there is a 33 per cent higher risk of chronic renal disease for every 5-year rise in age (Choi, 2008).

Cataracts are also a common complication in HSCT survivors. At 15-years post HSCT, the cumulative incidence of cataracts is 36 per cent (Gurney, 2006).

**Challenges in Use of SCT**

SCT is an essential treatment method for several blood-related disorders. However, its application is fraught with challenges that can significantly impact patient outcomes. This section explores these challenges, with a focus on clinical risk factors, the incidence of bloodstream infections (BSI), and associated risk factors during the post-transplant agranulocytosis phase.

Teshigawara-Tanabe et al. (2022) researched 55 patients with myelodysplastic syndromes who were receiving allogeneic SCT. They discovered various risk variables that negatively impact OS and event-free survival (EFS). Age 55 years or older, Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) more than 2, and intermediate or worse cytogenetic status before SCT were important factors indicating worse results. Additionally, an absolute neutrophil count of $<800/\mu L$ and elevated C-reactive protein levels before SCT, along with unrelated donor status, were associated with adverse OS and EFS rates. These findings underscore the importance of thorough pre-transplant assessments to identify patients at higher risk of poor outcomes.

Cao et al. (2021) highlighted the significant challenge of bloodstream infections (BSI) in the SCT context, especially during the agranulocytosis phase post-allogeneic transplantation. Out of 397 patients who underwent allogeneic stem cell transplantation, 17.7per cent experienced bloodstream infections while having low white blood cell counts. The infections were mainly caused by Gram-negative bacteria such Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa. The study found that pre-treatment with anti-thymocyte globulin (ATG), agranulocytosis lasting 21 days or more, and the source of stem cells are risk factors for BSI. The significant death rate (36.5 per cent) in patients with bloodstream infections highlights the urgent requirement for efficient infection control methods and customised antimicrobial treatments for this group of patients.

The challenges in SCT, particularly for patients with myelodysplastic syndromes and those undergoing allogeneic SCT, highlight the complex interplay of factors that influence post-transplant outcomes. Identifying and managing clinical risk factors before SCT is crucial for improving survival rates and reducing the incidence of complications such as BSI. Moreover, the findings from Cao et al. (2021) regarding the risk factors and pathogens involved in BSI during agranulocytosis provide valuable insights for developing targeted preventive and therapeutic interventions to mitigate this significant post-SCT complication.

Addressing the challenges associated with SCT, including clinical risk factors and the high incidence of BSI during agranulocytosis, is essential for optimizing patient outcomes. Ongoing research and clinical vigilance are imperative to identify at-risk populations and implement effective strategies to navigate these challenges effectively.

**CONCLUSION**

This literature review meticulously explored the existing research on SCT, from its foundational principles and historical milestones to its diverse applications and the challenges associated with its use.

In the pre-transplantation phase, meticulous planning is vital, involving donor selection and conditioning regimens customised to mitigate transplant-related risks while optimizing the graft's efficacy. This phase highlights the importance of tailored treatment approaches based on a comprehensive knowledge of the patient's individual medical history and the unique features of the condition.

SCT's utility spans a vast spectrum of applications, extending its medicinal reach beyond hematological malignancies to include autoimmune diseases and solid tumors. This versatility not only highlights SCT's potential to offer a lifeline to patients with otherwise stubborn conditions but also the variability in success rates and associated risks, necessitating a nuanced approach to patient selection and treatment planning.

The post-transplantation period is full of potential complications, including GVHD, opportunistic infections, and long-standing health issues. Effective management of these challenges is crucial to ensuring patient recovery and maintaining quality of life, emphasizing the importance of continuous care and vigilant monitoring post-SCT.

SCT has hurdles because to clinical risk factors that can affect outcomes and an elevated risk of complications including bloodstream infections during periods of agranulocytosis. These challenges

emphasise the need for a judicious approach to patient selection, meticulous treatment planning, and comprehensive post-transplant care.

The findings from this review show the intricate nature of SCT, necessitating an interdisciplinary approach that combines clinical expertise with a deep understanding of stem cell biology. For practitioners, the insights from this review will demonstrate the importance of adopting a patient-centric approach to SCT, taking into consideration the unique risk factors, disease pathology, and the dynamic landscape of SCT research. Theoretically, the review encourages the development of sophisticated predictive models to enhance clinical decision-making in SCT.

Various areas related to SCT can be studied by future researchers. These involve creating less harmful treatment plans, gaining a more thorough comprehension of GVHD causes and treatment, and investigating the possible uses of SCT in regenerative medicine. Additionally, efforts to improve post-transplant complications and address long-term health issues remain critical. The advent of gene editing and cellular therapies lead to the prospect of more targeted and successful SCT treatments.

Overall, SCT is a monumental leap in medical science, offering transformative treatments that have reshaped the medical landscape. As research and clinical efforts in this field continue to advance, the future of SCT holds the promise of more refined, safer, and broadly applicable stem cell-based interventions.

## REFERENCES


1. Ah Jung, I., Jeon, Y. J., Cho, W. K., Lee, J. W., Chung, N. G., Jung, M. H., Cho, B., & Suh, B. K. (2015). Development of diabetes mellitus after hematopoietic stem cell transplantation for childhood leukemia. International Journal of Pediatric Endocrinology, 2015(Suppl 1), P28. https://doi.org/10.1186/1687-9856-2015-S1-P28
2. Armenian, S. H., Sun, C. L., Vase, T., Ness, K. K., Blum, E., Francisco, L., Venkataraman, K., Samoa, R., Wong, F. L., Forman, S. J., & Bhatia, S. (2012). Cardiovascular risk factors in hematopoietic cell transplantation survivors: role in development of subsequent cardiovascular disease. Blood, 120(23), 4505–4512. https://doi.org/10.1182/blood-2012-06-437178
3. Bahena-Garcia M, Rivas-Vera S, Sobrevilla-Calvo P, Labardini-Mendez J, Cervera-Ceballos E, Calderon-Flores E. (2007). Hematopoietic stem cell transplantation in Multiple Myeloma. Experience of the Instituto Nacional de Cancerologia, Mexico. BMC Cancer, 5(7), A42. doi: 10.1186/1471-2407-7-S1-A42. PMCID: PMC1796588.s.
4. Baker, K. S., Ness, K. K., Steinberger, J., Carter, A., Francisco, L., Burns, L. J., Sklar, C., Forman, S., Weisdorf, D., Gurney, J. G., & Bhatia, S. (2007). Diabetes, hypertension, and cardiovascular events in survivors of hematopoietic cell transplantation: a report from the bone marrow transplantation survivor study. Blood, 109(4), 1765–1772. https://doi.org/10.1182/blood-2006-05-022335
5. Bennett J. S. (2005). Structure and function of the platelet integrin alphaIIbbeta3. The Journal of clinical investigation, 115(12), 3363–3369. https://doi.org/10. 1172/JCI26989
6. Bhatia S. (2011). Long-term health impacts of hematopoietic stem cell transplantation inform recommendations for follow-up. Expert review of hematology, 4(4), 437–454. https://doi.org/10.1586/ehm.11.39
7. Bhatia, S., Francisco, L., Carter, A., Sun, C. L., Baker, K. S., Gurney, J. G., McGlave, P. B., Nademanee, A., O'Donnell, M., Ramsay, N. K., Robison, L. L., Snyder, D., Stein, A., Forman, S. J., & Weisdorf, D. J. (2007). Late mortality after allogeneic hematopoietic cell transplantation and functional status of long-term survivors: report from the Bone Marrow Transplant Survivor Study. Blood, 110(10), 3784–3792. https://doi.org/10.1182/blood-2007-03-082933
8. Bhatia, M., & Sheth, S. (2015) Hematopoietic stem cell transplantation in sickle cell disease: patient selection and special considerations. Journal of Blood Medicine, 10(6), 229-238. DOI: 10.2147/JBM.S60515
9. Blyth, E., Withers, B., Clancy, L. & Gottlieb, D. (2016). CMV-specific immune reconstitution following allogeneic stem cell transplantation. Virulence, 7(8), 967-980. DOI: 10.1080/21505594.2016.1221022
10. Boeckh, M., Leisenring, W., Riddell, S. R., Bowden, R. A., Huang, M. L., Myerson, D., Stevens-Ayers, T., Flowers, M. E., Cunningham, T., & Corey, L. (2003). Late cytomegalovirus disease and mortality in recipients of allogeneic hematopoietic stem cell transplants: importance of viral load and T-cell immunity. Blood, 101(2), 407–414. https://doi.org/10.1182/blood-2002-03-0993
11. Brierley, C. K., Castilla-Llorente, C., Labopin, M., Badoglio, M., Rovira, M., Ricart, E., Dierickx, D., Vermeire, S., Hasselblatt, P., Finke, J., Onida, F., Cassinotti, A., Satsangi, J., Kazmi, M., López-Sanromán, A., Schmidt, C., Farge, D., Travis, S. P. L., Hawkey, C. J., Snowden, J. A., et al. (2018). European Society for Blood and Marrow Transplantation [EBMT] Autoimmune Diseases Working Party [ADWP]. Autologous Haematopoietic Stem Cell Transplantation for Crohn's Disease: A Retrospective Survey of Long-term Outcomes From the European Society for Blood and Marrow Transplantation. Journal of Crohn's & colitis, 12(9), 1097–1103. https://doi.org/10.1093/ecco-jcc/jjy069
12. Bryder, D., Rossi, D. J., & Weissman, I. L. (2006). Hematopoietic stem cells: the paradigmatic tissue-specific stem cell. The American journal of pathology, 169(2), 338–346. https://doi.org/10.2353/ajpath.2006.060312
13. Burkhardt, U. E., & Wu, C. J. (2013). Boosting leukemia-specific T cell responses in patients following stem cell transplantation. OncoImmunology, 2(11), e26587. DOI: 10.4161/onci.26587
14. Campbell, S., Sun, C. L., Kurian, S., Francisco, L., Carter, A., Kulkarni, S., Parker, P., Karanes, C., Forman, S. J., & Bhatia, S. (2009). Predictors of avascular necrosis of bone in long-term survivors of hematopoietic cell transplantation. Cancer, 115(18), 4127–4135. https://doi.org/10.1002/cncr.24474
15. Cao, W., Guan, L., Li, X., Zhang, R., Li, L., Zhang, S., Wang, C., Xie, X., Jiang, Z., Wan, D., & Chi, X. (2021). Clinical analysis of bloodstream infections during agranulocytosis after allogeneic hematopoietic stem cell transplantation. Infection and Drug Resistance, 14, 185-192. DOI: 10.2147/IDR.S280869
16. Carter, A., Robison, L. L., Francisco, L., Smith, D., Grant, M., Baker, K. S., Gurney, J. G., McGlave, P. B., Weisdorf, D. J., Forman, S. J., & Bhatia, S. (2006). Prevalence of conception and pregnancy outcomes after hematopoietic cell transplantation: report from the Bone Marrow Transplant Survivor Study. Bone marrow transplantation, 37(11), 1023–1029. https://doi.org/10.1038/sj.bmt.1705364
17. Cho, W. K., Cho, K. S., Park, S. H., Hahn, S. H., & Suh, B. K. (2013). Thyroid dysfunction after hematopoietic stem cell transplantation in children: older age and acute GVHD might be risk factors of thyroid dysfunction during 3 months after HSCT. International Journal of Pediatric Endocrinology, 2013(Suppl 1), P142. https://doi.org/10.1186/1687-9856-2013-S1-P142
18. Choi, M., Sun, C. L., Kurian, S., Carter, A., Francisco, L., Forman, S. J., & Bhatia, S. (2008). Incidence and predictors of delayed chronic kidney disease in long-term survivors of hematopoietic cell transplantation. Cancer, 113(7), 1580–1587. https://doi.org/10.1002/cncr.23773
19. Cordas Dos Santos, D. M., Saliba, R. M., Patel, R., Bashir, Q., Saini, N., Hosing, C., Kebriaei, P., Khouri, I. F., Nieto, Y., Popat, U., Ahmed, H., Lee, H. C., Manasanch, E. E., Patel, K. K., Thomas, S. K., Weber, D. M., Orlowski, R. Z., Champlin, R. E., & Qazilbash, M. H. (2020). Age Is a Prognostic Factor for the Overall Survival of Patients with Multiple Myeloma Undergoing Upfront Autologous Hematopoietic Stem Cell Transplantation. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation, 26(6), 1077–1083. https://doi.org/10.1016/j.bbmt.2019.11.028
20. Dai, J., Hight, R. S., Grullon, K., Xiao, T. L., & Stein, S. L. (2023). Vitiligo-like manifestations of graft-versus-host disease in a pediatric population. Pediatric Dermatoloy, 40(1), 157–161. doi:10.1111/pde.15121
21. Dawson, G., Sun, J. M., Davlantis, K. S., Murias, M., Franz, L., Troy, J., Simmons, R., Sabatos-DeVito, M., Durham, R., & Kurtzberg, J. (2017). Autologous Cord Blood Infusions Are Safe and Feasible in Young Children with Autism Spectrum Disorder: Results of a Single-Center Phase I Open-Label Trial. Stem cells translational medicine, 6(5), 1332–1339. https://doi.org/10.1002/sctm.16-0474
22. De Bruin, M. L., Huisbrink, J., Hauptmann, M., Kuenen, M. A., Ouwens, G. M., van't Veer, M. B., Aleman, B. M., & van Leeuwen, F. E. (2008). Treatment-related risk factors for premature menopause following Hodgkin lymphoma. Blood, 111(1), 101–108. https://doi.org/10.1182/blood-2007-05-090225
23. Dessie, G., Derbew Molla, M., Shibabaw, T, & Ayelign, B. (2020). Role of stem-cell transplantation in Leukemia treatment. Stem Cells and Cloning: Advances and Applications, 13, 67-77, DOI: 10.2147/SCCAA.S262880
24. Doubrovina, E., Oflaz-Sozmen, B., Prockop, S. E., Kernan, N. A., Abramson, S., Teruya-Feldstein, J., Hedvat, C., Chou, J. F., Heller, G., Barker, J. N., Boulad, F., Castro-Malaspina, H., George, D., Jakubowski, A., Koehne, G., Papadopoulos, E. B., Scaradavou, A., Small, T. N., Khalaf, R., Young, J. W., … O'Reilly, R. J. (2012). Adoptive immunotherapy with unselected or EBV-specific T cells for biopsy-proven EBV+ lymphomas after allogeneic hematopoietic cell transplantation. Blood, 119(11), 2644–2656. https://doi.org/10.1182/blood-2011-08-371971
25. Fiore, M., Nurden, A. T., Nurden, P., & Seligsohn, U. (2012). Clinical utility gene card for: Glanzmann thrombasthenia. European journal of human genetics, 20(10). https://doi.org/10.1038/ejhg.2012.151
26. Fung, H. C., Nathan, S., & Maciejewski, J. J. (2010). Induction chemotherapy before autologous stem cell transplantation for symptomatic plasma cell myeloma – does it matter? Clinical Pharmacology: Advances and Applications, 2, 71-75. DOI: 10.2147/CPAA.S6258
27. Guedes, M., Zilhão, C., Palhau, L., Almeida, I., Silva, I., Vasconcelos, C., Marinho, A., Vaz, C., & Campos, A. (2013). PReS-FINAL-2122: Autologous stem cell transplantation in a patient with severe systemic sclerosis in Portugal. Pediatric Rheumatology Online Journal, 11(Suppl 2), P134. https://doi.org/10.1186/1546-0096-11-S2-P134
28. Gulati, S. C., & Van Poznak, C. (1998). Pregnancy after bone marrow transplantation. Journal of clinical oncology, 16(5), 1978–1985.https://doi.org/10. 1200/JCO.1998.16.5.1978
29. Gurney, J. G., Ness, K. K., Rosenthal, J., Forman, S. J., Bhatia, S., & Baker, K. S. (2006). Visual, auditory, sensory, and motor impairments in long-term survivors of hematopoietic stem cell transplantation performed in childhood: results from the Bone Marrow Transplant Survivor study. Cancer, 106(6), 1402–1408. https://doi.org/10.1002/cncr.21752
30. Gyurkocza, B., Rezvani, A., & Storb, R. F. (2010). Allogeneic hematopoietic cell transplantation: the state of the art. Expert Reviews in Hematology, 3(3), 285–299. doi:10.1586/ehm.10.21
31. Harris, A. E., Styczynski, J., Bodge, M., Mohty, M., Savani, B. N., & Ljungman, P. (2015). Pretransplant vaccinations in allogeneic stem cell transplantation donors and recipients: an often-missed opportunity for immunoprotection? Bone marrow transplantation, 50(7), 899–903. https://doi.org/10.1038/bmt.2015.49
32. Harris, B., Morjaria, S. M., Littmann, E. R., Geyer, A. I., Stover, D. E., Barker, J. N., Giralt, S. A., Taur, Y., & Pamer, E. G. (2016). Gut Microbiota Predict Pulmonary Infiltrates after Allogeneic Hematopoietic Cell Transplantation. American Journal of Respiratory and Critical Care Medicine, 194(4), 450–463. https://doi.org/10.1164/rccm.201507-1491OC
33. Hatzimichael, E. & Tuthill, M. (2010). Hematopoietic stem cell transplantation. Stem Cells and Cloning: Advances and Applications, 26(3), 105-117. DOI: 10.2147/SCCAA.S6815
34. Hirabayashi, K., Nakazawa, Y., Matsuura, H., Hara, Y., Kurata, T., Hirabayashi, K., Saito, S., Yoshikawa, K., Tanaka, M., Yanagisawa, R., Sakashita, K., & Koike, K. (2014). Risk factors for diabetes mellitus and impaired glucose tolerance following allogeneic hematopoietic stem cell transplantation in pediatric patients with hematological malignancies. International journal of hematology, 99(4), 477–486. https://doi.org/10.1007/s12185-014-1536-8
35. Holzer, U., Tzaribachev, N., Kuemmerle-Deschner, J., Well, C., Lang, P., Handgretinger, R., & Mueller, I. (2008). Successful autologous stem cell transplantation (ASCT) in a patient with juvenile dermatomyositis. Pediatric Rheumatology Online Journal, 6(1), P221. https://doi.org/10.1186/1546-0096-6-S1-P221
36. Hu, Y., Jiang, Y., Liu, S., Shen, J., & An, Y. (2021). Phenotypes, lung microbiota and cytokine responses in pneumonia after hematopoietic stem cell transplantation. Journal of Inflammation Research, 14, 6055-6065. DOI: 10.2147/ JIR.S338914
37. Jadoul, P., & Donnez, J. (2012). How does bone marrow transplantation affect ovarian function and fertility?. Current opinion in obstetrics & gynecology, 24(3), 164–171. https://doi.org/10.1097/GCO.0b013e328353bb57
38. Jenq, R. R., Ubeda, C., Taur, Y., Menezes, C. C., Khanin, R., Dudakov, J. A., Liu, C., West, M. L., Singer, N. V., Equinda, M. J., Gobourne, A., Lipuma, L., Young, L. F., Smith, O. M., Ghosh, A., Hanash, A. M., Goldberg, J. D., Aoyama, K., Blazar, B. R., Pamer, E. G., … van den Brink, M. R. (2012). Regulation of intestinal inflammation by microbiota following allogeneic bone marrow transplantation. The Journal of experimental medicine, 209(5), 903–911. https://doi.org/10.1084/jem.20112408
39. Kaste, S. C., Shidler, T. J., Tong, X., Srivastava, D. K., Rochester, R., Hudson, M. M., Shearer, P. D., & Hale, G. A. (2004). Bone mineral density and osteonecrosis in survivors of childhood allogeneic bone marrow transplantation. Bone marrow transplantation, 33(4), 435–441. https://doi.org/10.1038/sj.bmt.1704360
40. Kersting, S., Hené, R. J., Koomans, H. A., & Verdonck, L. F. (2007). Chronic kidney

disease after myeloablative allogeneic hematopoietic stem cell transplantation. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation, 13(10), 1169–1175. https://doi.org/10. 1016/j.bbmt.2007.06.008
41. Kharfan-Dabaja, M. A., Boeckh, M., Wilck, M. B., Langston, A. A., Chu, A. H., Wloch, M. K., Guterwill, D. F., Smith, L. R., Rolland, A. P., & Kenney, R. T. (2012). A novel therapeutic cytomegalovirus DNA vaccine in allogeneic haemopoietic stem-cell transplantation: a randomised, double-blind, placebo-controlled, phase 2 trial. The Lancet. Infectious diseases, 12(4), 290–299. https://doi.org/10.1016/S1473-3099(11)70344-9
42. Leen, A. M., Bollard, C. M., Mendizabal, A. M., Shpall, E. J., Szabolcs, P., Antin, J. H., Kapoor, N., Pai, S. Y., Rowley, S. D., Kebriaei, P., Dey, B. R., Grilley, B. J., Gee, A. P., Brenner, M. K., Rooney, C. M., & Heslop, H. E. (2013). Multicenter study of banked third-party virus-specific T cells to treat severe viral infections after hematopoietic stem cell transplantation. Blood, 121(26), 5113–5123. https://doi.org/10.1182/blood-2013-02-486324
43. Ljungman, P., Bermudez, A., Logan, A. C., Kharfan-Dabaja, M. A., Chevallier, P., Martino, R., Wulf, G., Selleslag, D., Kakihana, K., Langston, A., Lee, D. G., Solano, C., Okamoto, S., Smith, L. R., Boeckh, M., Wingard, J. R., Cywin, B., Fredericks, C., Lademacher, C., Wang, X., … Maertens, J. (2021). A randomised, placebo-controlled phase 3 study to evaluate the efficacy and safety of ASP0113, a DNA-based CMV vaccine, in seropositive allogeneic haematopoietic cell transplant recipients. EClinicalMedicine, 33, 100787. https://doi.org/10.1016/j.eclinm.2021.100787
44. Loren, A. W., & Senapati, S. (2019). Fertility preservation in patients with hematologic malignancies and recipients of hematopoietic cell transplants. Blood, 134(9), 746–760. https://doi.org/10.1182/blood.2018846790
45. Lyu, M., Jiang, E., He, Y., Yang, D., Ma, Q., Pang, A., Zhai, W., Wei, J., Huang, Y., Zhang, G., Zhang, R., Feng, S., & Han, M. (2021). Comparison of autologous and allogeneic stem cell transplantation for patients with Philadelphia chromosome-positive acute lymphoblastic leukemia. Hematology, 26(1), 65-74. DOI: 10.1080/16078454.2020.1868783
46. Lv, Y. T., Zhang, Y., Liu, M., Qiuwaxi, J. N., Ashwood, P., Cho, S. C., Huan, Y., Ge, R. C., Chen, X. W., Wang, Z. J., Kim, B. J., & Hu, X. (2013). Transplantation of human cord blood mononuclear cells and umbilical cord-derived mesenchymal stem cells in autism. Journal of Translational Medicine, 11, 196. https://doi.org/10.1186/1479-5876-11-196
47. Magurran, A. E. (2004). Measuring biological diversity. Malden, MA: Blackwell Publishing.
48. Majhail, N. S., Flowers, M. E., Ness, K. K., Jagasia, M., Carpenter, P. A., Arora, M., Arai, S., Johnston, L., Martin, P. J., Baker, K. S., Lee, S. J., & Burns, L. J. (2009). High prevalence of metabolic syndrome after allogeneic hematopoietic cell transplantation. Bone Marrow Transplantation, 43(1), 49–54. https://doi.org/10.1038/bmt.2008.263
49. Majhail, N. S., Ness, K. K., Burns, L. J., Sun, C. L., Carter, A., Francisco, L., Forman, S. J., Bhatia, S., & Baker, K. S. (2007). Late effects in survivors of Hodgkin and non-Hodgkin lymphoma treated with autologous hematopoietic cell transplantation: a report from the bone marrow transplant survivor study. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation, 13(10), 1153–1159. https://doi.org/10.1016/j.bbmt.2007.06.003
50. Mallhi, K. K., Petrovic, A., & Ochs, H. D. (2021). Hematopoietic Stem Cell Therapy for Wiskott–Aldrich Syndrome: Improved Outcome and Quality of Life. Journal of Blood Medicine, 11(12), 435-447, DOI: 10.2147/JBM.S232650
51. Martino, M., & Morabito, F. (2015). Autologous stem cell transplantation in multiple myeloma is not dead but alive and well. Expert Opinion On Biological Therapy, 15(2), 149–154. https://doi.org/10.1517/14712598.2015.988611
52. Mattano L. A., Jr (2004). Strategic approaches to osteoporosis in transplantation. Pediatric Transplantation, 8(5), 51–55. https://doi.org/10.1111/j.1398-2265.2004.00184.x
53. Moore, T. (2023). Hematopoietic Stem Cell Transplantation (HSCT). Medscape. Available at https://emedicine.medscape.com/article/208954-overview#a1
54. Nabetani, M., Mukai, T., Taguchi, A. (2023). Cell Therapies for Autism Spectrum Disorder Based on New Pathophysiology: A Review. Cell Transplantation, 32(1). doi:10.1177/09636897231163217
55. Nguyen, Q., Champlin, R., Giralt, S., Rolston, K., Raad, I., Jacobson, K., Ippoliti, C., Hecht, D., Tarrand, J., Luna, M., & Whimbey, E. (1999). Late cytomegalovirus pneumonia in adult allogeneic blood and marrow transplant recipients. Clinical infectious diseases,28(3), 618–623. https://doi.org/10.1086/515146
56. Nurden, A. T., Pillois, X., & Wilcox, D. A. (2013). Glanzmann thrombasthenia: State of the art and future directions. Seminars in Thrombosis and Hemostasis, 39(6), 642–655. https://doi.org/10.1055/s-0033-1353393
57. Ozsahin, H., Cavazzana-Calvo, M., Notarangelo, L. D., Schulz, A., Thrasher, A. J., Mazzolari, E., Slatter, M. A., Le Deist, F., Blanche, S., Veys, P., Fasth, A., Bredius, R., Sedlacek, P., Wulffraat, N., Ortega, J., Heilmann, C., O'Meara, A., Wachowiak, J., Kalwak, K., Matthes-Martin, S., … Fischer, A. (2008). Long-term outcome following hematopoietic stem-cell transplantation in Wiskott-Aldrich syndrome: collaborative study of the European Society for Immunodeficiencies and European Group for Blood and Marrow Transplantation. Blood, 111(1), 439–445. https://doi.org/10.1182/blood-2007-03-076679
58. Palumbo, A., Cavallo, F., Gay, F., Di Raimondo, F., Ben Yehuda, D., Petrucci, M. T., Pezzatti, S., Caravita, T., Cerrato, C., Ribakovsky, E., Genuardi, M., Cafro, A., Marcatti, M., Catalano, L., Offidani, M., Carella, A. M., Zamagni, E., Patriarca, F., Musto, P., Evangelista, A., … Cavo, M. (2014). Autologous transplantation and maintenance therapy in multiple myeloma. The New England journal of medicine, 371(10), 895–905. https://doi.org/10.1056/NEJMoa1402888
59. Parikh, C. R., McSweeney, P. A., Korular, D., Ecder, T., Merouani, A., Taylor, J., Slat-Vasquez, V., Shpall, E. J., Jones, R. B., Bearman, S. I., & Schrier, R. W. (2002). Renal dysfunction in allogeneic hematopoietic cell transplantation. Kidney International, 62(2), 566–573. https://doi.org/10.1046/j.1523-1755.2002.00455.x
60. Patriarca, F., Skert, C., Bonifazi, F., Sperotto, A., Fili, C., Stanzani, M., Zaja, F., Cerno, M., Geromin, A., Bandini, G., Baccarani, M., & Fanin, R. (2006). Effect on survival of the development of late-onset non-infectious pulmonary complications after stem cell transplantation. Haematologica, 91(9), 1268–1272.
61. Persoon, S., Kersten, M. J., van der Weiden, K., Buffart, L. M., Nollet, F., Brug, J., & Chinapaw, M. J. (2013). Effects of exercise in patients treated with stem cell transplantation for a hematologic malignancy: A systematic review and meta-analysis. Cancer Treatment Reviews, 39, 682–690.
62. Petryk, A., Bergemann, T. L., Polga, K. M., Ulrich, K. J., Raatz, S. K., Brown, D. M., Robison, L. L., & Baker, K. S. (2006). Prospective study of changes in bone mineral density and turnover in children after hematopoietic cell transplantation. The Journal of clinical endocrinology and metabolism, 91(3), 899–905. https://doi.org/10.1210/jc.2005-1927
63. Ruan, X. (2023) Expert consensus on fertility preservation in hematopoietic stem cell transplantation in girls in China. Gynecological Endocrinology, 39(1), 2146671. DOI: 10.1080/09513590.2022.2146671
64. Ruiz, M. A Kaiser, R. L. J., de Quadros, L. G., Caseiro, G. H. X., Oliveira, A. F., Peña-Arciniegas, T., Piron-Ruiz, L., Kaiser, F. S. L., & Oliveira, V. L. (2017). Hematopoietic stem cell transplantation in a severe refractory Crohn's disease patient with intestinal stoma: a case report. International Medical Case Reports Journal,10, 353-359. DOI: 10.2147/IMCRJ.S139552
65. Sanders, J. E. (1991). The impact of marrow transplant preparative regimens on subsequent growth and development. The Seattle Marrow Transplant Team. Seminars in Hematology, 28(3), 244–249.
66. Sanders, J. E., Buckner, C. D., Amos, D., Levy, W., Appelbaum, F. R., Doney, K., Storb, R., Sullivan, K. M., Witherspoon, R. P., & Thomas, E. D. (1988). Ovarian function following marrow transplantation for aplastic anemia or leukemia. Journal of Clinical Oncology, 6(5), 813–818. https://doi.org/10.1200/JCO.1988.6.5.813
67. Sanli, H., Akay, B. N., Arat, M., et al. (2008). Vitiligo after hematopoietic cell transplantation: Six cases and review of the literature. Dermatology, 216(4), 349–354. doi:10.1159/000117705
68. Shimoni, A., Hardan, I., Shem-Tov, N., et al. (2006). Allogeneic hematopoietic stem-cell transplantation in AML and MDS using myeloablative versus reduced-intensity conditioning: the role of dose intensity. Leukemia, 20(2):322. doi:10.1038/sj.Leu.2404037
69. Santoro, N., Ruggeri, A., Labopin, M., et al. (2017). Unmanipulated haploidentical stem cell transplantation in adults with acute lymphoblastic leukemia: A study on behalf of the Acute Leukemia Working Party of the EBMT. Journal of Hematology and Oncoloy, 10(1), 113. doi:10.1186/s13045-017-0480-5
70. Shizuru, J. A., Negrin, R. S., & Weissman, I. L. (2005). Hematopoietic stem and progenitor cells: Clinical and preclinical regeneration of the hematolymphoid system. Annual Review of Medicine, 56, 509–538. https://doi.org/10.1146/annurev.med.54.101601.152334
71. Socié, G., Salooja, N., Cohen, A., Rovelli, A., Carreras, E., Locasciulli, A., Korthof, E., Weis, J., Levy, V., Tichelli, A., & Late Effects Working Party of the European Study Group for Blood and Marrow Transplantation (2003). Nonmalignant late effects after allogeneic stem cell transplantation. Blood, 101(9), 3373–3385. https://doi.org/10.1182/blood-2002-07-2231
72. Solh, T., Botsford, A., & Melhem Solh, M. (2015). Glanzmann's Thrombasthenia: Pathogenesis, diagnosis, and current and emerging treatment options. Journal of Blood Medicine, 8(6), 219-227, DOI: 10.2147/JBM.S71319
73. Syrjala, K. L., Langer, S. L., Abrams, J. R., Storer, B. E., & Martin, P. J. (2005). Late effects of hematopoietic cell transplantation among 10-year adult survivors compared with case-matched controls. Journal of Clinical Oncology, 23(27), 6596–6606. https://doi.org/10.1200/JCO.2005.12.674
74. Taur, Y., Jenq, R. R., Perales, M. A., Littmann, E. R., Morjaria, S., Ling, L., No, D., Gobourne, A., Viale, A., Dahi, P. B., Ponce, D. M., Barker, J. N., Giralt, S., van den Brink, M., & Pamer, E. G. (2014). The effects of intestinal tract bacterial diversity on mortality following allogeneic hematopoietic stem cell transplantation. Blood, 124(7), 1174–1182. https://doi.org/10.1182/blood-2014-02-554725
75. Taur, Y., Xavier, J. B., Lipuma, L., Ubeda, C., Goldberg, J., Gobourne, A., Lee, Y. J., Dubin, K. A., Socci, N. D., Viale, A., Perales, M. A., Jenq, R. R., van den Brink, M. R., & Pamer, E. G. (2012). Intestinal domination and the risk of bacteremia in patients undergoing allogeneic hematopoietic stem cell transplantation. Clinical Infectious Diseases, 55(7), 905–914. https://doi.org/10.1093/cid/cis580
76. Teshigawara-Tanabe, H., Hagihara, M., Aoki, J., Koyama, S., Takahashi, H., Nakajima, Y., Kunimoto, H., Tachibana, T., Miyazaki, T., Matsumoto, K., Tanaka, M., Yamazaki, E., Fujisawa, S., Kanamori, H., Taguri, M., & Nakajima, H. (2022) Clinical risk factors for patients with myelodysplastic syndromes undergoing allogeneic hematopoietic stem cell transplantation. Hematology, 27(1), 620-628. DOI: 10.1080/16078454.2022.2052601
77. Uchimaru, K., Ohno, N., Kobayashi, S. et al. (2015). Early hematopoietic stem cell transplantation improve treatment outcome of aggressive ATL. Retrovirology, 12(1), P28 https://doi.org/10.1186/1742-4690-12-S1-P28
78. van Haren, I. E. P. M., Timmerman, H., Potting, C. M., Blijlevens, N. M., Staal, J. B., Nijhuis-van der Sanden, M.W. (2013). Physical exercise for patients undergoing hematopoietic stem cell transplantation: Systematic review and meta-analyses of randomized controlled trials. Physical Therapy, 93, 514–528.
79. van Haren, I. E. P. M., staal, J. B., Potting, C. M., Atsma, F., Hoogeboom, T. J., Nicole M. A. Blijlevens & Maria W. G. Nijhuis-van der Sanden. (2018). Physical exercise prior to hematopoietic stem cell transplantation: A feasibility study. Physiotherapy Theory and Practice, 34(10), 747-756. DOI: 10.1080/09593985.2018.1423655
80. Wang, Y., Hu, W., Lin, F., & Xu, A. (2023). Generalized vitiligo after stem cell transplantation: A case report. Clinical, Cosmetic and Investigational Dermatology, 16, 1945-1948. DOI: 10.2147/CCID.S420342
81. Weisdorf, D. J., Nelson, G., Lee, S. J., Haagenson, M., Spellman, S., Antin, J. H., Bolwell, B., Cahn, J. Y., Cervantes, F., Copelan, E., Gale, R., Gratwohl, A., Khoury, H. J., McCarthy, P., Marks, D. I., Szer, J., Woolfrey, A., Cortes-Franco, J., Horowitz, M. M., Arora, M., … Chronic Leukemia Working Committee (2009). Sibling versus unrelated donor allogeneic hematopoietic cell transplantation for chronic myelogenous leukemia: refined HLA matching reveals more graft-versus-host disease but not less relapse. Biology of Blood And Marrow Transplantation, 15(11), 1475–1478. https://doi.org/10.1016/j.bbmt.2009.06.016
82. Xiong, W., & Derk, C. T. (2009) Treatment of systemic sclerosis: potential role for stem cell transplantation. Stem Cells and Cloning: Advances and Applications,18(2), 1-9. DOI: 10.2147/sccaa.s5282
83. Yoshihara, S., Yanik, G., Cooke, K. R., & Mineishi, S. (2007). Bronchiolitis obliterans syndrome (BOS), bronchiolitis obliterans organizing pneumonia (BOOP), and other late-onset noninfectious pulmonary complications following allogeneic hematopoietic stem cell transplantation. Biology of Blood and Marrow Transplantation, 13(7), 749–759. https://doi.org/10.1016/j.bbmt.2007.05.001
84. Zhu, J., Su, G., Lai, J., Dong, B., Kang, M., Li, S., Zhou, Z., & Wu, F. (2018). Long-term follow-up of autologous hematopoietic stem cell transplantation for refractory juvenile dermatomyositis: a case-series study. Pediatric Rheumatology Online Journal, 16(1), 72. https://doi.org/10.1186/s12969-018-0284-3