

Dispelling Potential Fears Associated with Stem Cell Donation

AN EVIDENCE-BASED COMMENTARY

ALEXANDER E. ANAGNOSTOPOULOS¹,
OWEN BARIBEAU², ALI ESHAGHPOUR³, YUJIA
(JULIA) GUO², ANNA LEE³, OWEN DAN LUO²

¹Bachelor of Health Sciences (Honours) Class of 2018, McMaster University

²Bachelor of Health Sciences (Honours) Class of 2019, McMaster University

³Bachelor of Health Sciences (Honours) Class of 2020, McMaster University
Correspondence: luoo@mcmaster.ca

ABSTRACT

An increasing number of patients require life-saving stem cell transplants, often from unrelated donors. In order to facilitate this process, bone marrow and stem cell registries have been established to genetically catalog potential donors and can be used to find matches for patients in need. Given the wide genetic variability in populations and significant ethnic disparities in donor registries worldwide, there are substantial gaps in the availability of compatible unrelated stem cell donors. Limited understanding of the procedures involved in stem cell donation, along with potential misconceptions of associated risks, may discourage prospective donors. Many people are unaware that there are two established methods for stem cell donation from adult donors, either through bone marrow harvest or—more commonly—through peripheral blood stem cell harvest. This evidence-based commentary explores these two procedures, deconstructs misconstrued fears associated with stem cell donation, and subsequently encourages readers to consider registering as stem cell donors.

may be explained by 2017 data revealing that only 1% of Canadians are currently registered as stem cell donors.⁶ Additionally, although patients are more likely to find matches within their own ethnic group, there is a lack of ethnic diversity in donor registries, with non-caucasians comprising only 31% of the OneMatch Registry, as of January 2017.⁷ As a result, the probability of finding a suitable donor varies greatly depending on patient ethnicity, from 75% for Caucasian patients to 27% for African-American patients.⁷ The resulting discrepancy highlights the need for more ethnically diverse donors.⁷

COMMON FEARS ASSOCIATED WITH STEM CELL DONATION

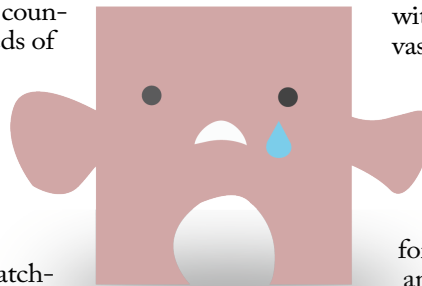
Literature reports that fear and lack of understanding of stem cell donation represent barriers for donor registration.^{8,9} Individuals informed about the donation process are more likely to participate as stem cell donors; thematic syntheses of qualitative investigations on donor motivations reveal that fear of invasive procedures is a primary concern in their decision.¹⁰ According to psychosocial assessments of prospective bone marrow donors, the possibility of postoperative paralysis or death during the operation induces substantial anxiety.¹¹ This is evident from statements such as, “I thought of an operation on the spine, that I could not walk anymore,” or “I thought that you might have died through it. I didn’t know that you could make more bone marrow.” These fears are perpetuated by the popular misconception that the bone marrow is the sole source of stem cells for transplantation; in reality, stem cells can be collected from the periphery with the more common and less invasive method of PBSC-T.¹²

Nonetheless, the idea of PBSC-T elicits its own fears. The drug granulocyte colony-stimulating factor (G-CSF) is instrumental in PBSC donation, for which blood is filtered through an apheresis machine to extract stem cells. Before the two to six hour donation procedure, G-CSF is

INTRODUCTION

For patients with a range of conditions - including blood cancers, autoimmune disorders, and metabolic diseases - hematopoietic stem cell transplants may be an integral component of their treatment.¹ Medical literature has extensively detailed the benefits of these procedures, namely their potential to significantly increase patient survival and long-term quality of life.² Unfortunately, the requirement of genetic compatibility between donor and recipient and the reality of related donors found by fewer than 30% of patients leave the remaining 70% of patients to search for a compatible unrelated donor in a national registry.³ These donors will altruistically provide stem cells through one of two methods: bone marrow transplantation (BMT) or peripheral blood stem cell transplantation (PBSC-T). In Canada, the OneMatch Stem Cell and Bone Marrow registry collaborates with 75 registries in 53 other countries to facilitate hundreds of annual matches.⁴

Despite these efforts, nearly half of the Canadian patients in need of stem cell transplants are still unable to find a matching donor.⁵ This disconnect between supply and demand



1. Passweg JR, Halter J, Bucher C, Gerull S, Heim D, Rovó A et al. Hematopoietic stem cell transplantation: a review and recommendations for follow-up care for the general practitioner. *Swiss Med Wkly*. 2012;142:w13696.
2. Grulke N, Albani C, Bailor H. Quality of life in patients before and after haematopoietic stem cell transplantation measured with the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Core Questionnaire QLQ-C30. *Bone Marrow Transplant*. 2012;47(4):473.
3. Kopolovic I, Turner R. Donation and transplantation of allogeneic hematopoietic stem cells. *CMAJ*. 2011;183(17):2014.
4. Adler J. Donation & Transplantation at Canadian Blood Services. [Presentation] Nova Scotia Provincial Blood Coordinating Program. 6th November 2015. Available from: <https://novascotia.ca/dhw/nsbpcp/docs/Donation-and-Transplantation-at-Canadian-Blood-Services.pdf> [Accessed 3rd January 2018].
5. Smith S. OneMatch Network Overview and Stem Cell/Bone Marrow Transplantation [Presentation]. *Canadian Blood Services*. Oct 2010. Available from: <https://novascotia.ca/dhw/nsbpcp/docs/OneMatch-Network-Overview-and-Transplantation.pdf> [Accessed 3rd January 2018].
6. Fingrut W, Parmar S, Cuperfain A, Rikhray K, Charman E, Ptak E, Kahlon M, Graham A, Luong S, Wang YG, Yu J. The Stem Cell Club: a model for unrelated stem cell donor recruitment. *Transfusion*. 2017 Dec 1;57(12):2928-36. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/28944484> [Accessed 3rd January 2018].
7. Institute for Justice. Bone Marrow Statistics. Available from: <http://ij.org/bonemarrowstatistics/> [Accessed 3rd January 2018].
8. Onitilo AA, Lin YH, Okonofua EC, Afrin LB, Arai J, Tilley BC. Race, education and knowledge of bone marrow registry: indicators of willingness to donate bone marrow among African Americans and Caucasians. *Transplant Proc*. 2004; 36(10):3212-9.
9. Kollman C, Weis T, Switzer GE, Halet M, Kitajima D, Hegland J et al. Non-HLA barriers to unrelated donor stem cell transplantation. *Bone Marrow Transplant*. 2001;27(6):581.
10. Garcia MC, Chapman JR, Shaw RJ, Gottlieb DJ, Ralph A, Craig JC et al. Motivations, experiences, and perspectives of bone marrow and peripheral blood stem cell donors: thematic synthesis of qualitative studies. *Biol Blood Marrow Transplant*. 2013;19(7):1046-58.
11. McLaren PJ, Hyde MK, White KM. Exploring the role of gender and risk perceptions in people's decisions to register as a bone marrow donor. *Health Educ Res*. 2011;27(3):513-22.

administered to greatly increase the count of hematopoietic stem cells in the bloodstream.¹³ Prospective PBSC donors are reportedly wary of side effects associated with G-CSF drug administration.^{14,15} Furthermore, an online survey exploring public awareness of stem cell donation found that approximately 31% of the 1,471 participants against joining a stem cell registry worried that the PBSC donation process would be painful.¹⁶

“Evidence indicates a low overall risk for bone marrow donors, suggesting that many reported fears may be exaggerated.”

ADDRESSING FEARS ASSOCIATED WITH STEM CELL DONATION

Evidence indicates a low overall risk for bone marrow donors, suggesting that many reported fears may be exaggerated. Bone marrow donation involves the extraction of stem cells from the hip bone, rather than the spine.¹⁷ Moreover, bone marrow donation is a day surgery performed under general anaesthetic, with most donors discharged from the hospital within 24 hours.^{17,18} An investigation into the major adverse events associated with bone marrow donation revealed only one death and zero cases of paralysis in a large sample of 27,770 donors.¹⁹ Although pain at the anatomical site of donation is self-reported by 82% of donors, this symptom is amenable to anti-inflammatory drug therapy, with a median recovery time of three weeks.^{17,18} This evidence suggests that the risks associated with bone marrow donation are overall low.

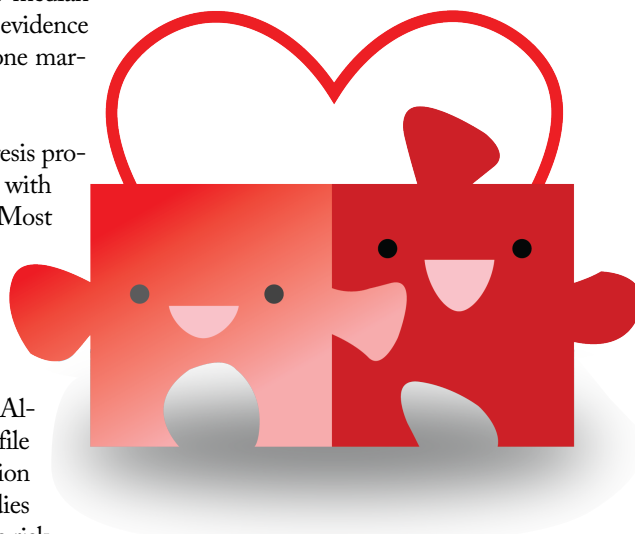
Furthermore, PBSC-T employs an apheresis procedure that is well-documented to be safe with a very low risk of serious adverse effects.²⁰ Most recipients experience short-term side effects from G-CSF injections, such as bone pain, nausea, and fatigue.^{18,21,22} However, the median recovery time for PBSC donors is one week, with 94% of donors fully recovering after 30 days.¹⁸ Although the long-term (>10 years) risk profile of G-CSF treatment and PBSC donation remains to be elucidated, prospective studies suggest that G-CSF does not increase the risk for leukemia or other hematopoietic malignancies

relative to unexposed controls.^{23,24}

STEM CELL DONATION MATTERS

Regardless of the method for stem cell donation, recipient prognosis significantly improves, whereas life expectancies for individuals unable to receive stem cell therapies deteriorates.²⁵ Among a sample of adult patients with previous blood cancer who became cancer-free two years after transplantation, after transplantation, the probability of five-year survival was 89%. Additionally, for the patients who remained disease-free, rate of survival 20 years after transplantation was estimated at 80.4%.²⁶

The long-term health benefits of stem cell transplants, compared to those of the non-transplant alternative, are substantial, but they are unfortunately unattainable for many patients. Given that the number of Canadian patients in need of unrelated donors is only increasing, we hope that our review, with its examination of the low overall risks associated with stem cell donation and the promising outcomes for recipients, dispels potential fears associated with the procedure and inspires individuals to register as stem cell donors. In fact, the number of patients in need of unrelated donors is only increasing in Canada.²⁷ We hope that our review outlining the low overall risks associated with stem cell donation and the promising outcomes for recipients of stem cell therapies dispels potential fears associated with donation procedures and inspires individuals to register as stem cell donors.



ARTIST
MATILDA KIM

REVIEWED BY DR. WARREN FINGRUT

EDITED BY TAKHLIQ AMIR & SHIKHA PATEL

Dr. Warren Fingrut is an internal medicine resident physician at the University of Toronto. He is the founder and director of Stem Cell Club, a non-profit organization that aims to improve membership on Canada's stem cell donor database. He has published on topics pertaining to unrelated donor recruitment in the journals, *Transfusion* and *Vox Sanguinis*.

12. D'Souza A, Fritham C. Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides. *Center for International Blood & Marrow Transplant Research*. 2017. Available from: <http://www.cibmtr.org> [Accessed 15th February 2018].
13. Billen A, Madrigal J, Scior K, Shaw B, and Strydom A. Donation of peripheral blood stem cells to unrelated strangers: A thematic analysis. *PLoS One*. 2017;12(10):e0186438.
14. van Walraven SM, Ball LM, Koopman, HM et al. Managing a dual role—experiences and coping strategies of parents donating haploidentical G-CSF mobilized peripheral blood stem cells to their children. *Psycho-Oncol*. 2012; 21: 168–175.
15. Pillay B, Lee S, Katona, L. et al. The psychosocial impact of hematopoietic SCT on sibling donors. *Bone Marrow Transplant*. 2012; 47: 1361–1365.
16. Anthony Nolan Stem Cell Donation Poll. *ComRes*. 2011 p. 15-16. Available from: <http://www.comresglobal.com/polls/anthony-nolan-stem-cell-donation-poll/> [Accessed 11th February 2018].
17. Nishimori M, Yamada Y, Hoshi K, Akiyama Y, Hoshi Y, Morishima Y et al. Health-related quality of life of unrelated bone marrow donors in Japan. *Blood*. 2002;99(6):1995-2001.
18. Miller JP, Perry EH, Price TH, Bolan GD, Karanes C, Boyd TM et al. Recovery and safety profiles of marrow and PBSC donors: experience of the National Marrow Donor Program. *Biol Blood Marrow Transplant*. 2008;14(9 Suppl):29-36.
19. Halter J, Kodera Y, Ispizua ALJ, Greinix HT, Schmitz N, Favre G et al. Severe events in donors after allogeneic hematopoietic stem cell donation. *Haematologica*. 2009;94(1):94-101.
20. Philip J, Sarkar RS, Pathak A. Adverse events associated with apheresis procedures: incidence and relative frequency. *Asian J Transfus Sci*. 2013;1(1):37.
21. Anderlini P, Przepiorka D, Seong D, Miller P, Sundberg J, Lichtiger B et al. Clinical toxicity and laboratory effects of granulocyte colony-stimulating factor (filgrastim) mobilization and blood stem cell apheresis from normal donors, and analysis of charges for the procedures. *Transfusion*. 1996;36(7):590-595.
22. McCullough J, Kahn J, Adamson J, Anderlini P, Benjamin R, Confer D et al. Hematopoietic growth factors—use in normal blood and stem cell donors: clinical and ethical issues. *Transfusion*. 2008;48(9):2008-2025.
23. Confer D, Miller J. Long-term safety of filgrastim (rhG-CSF) administration. *Br J Haematol*. 2007;137(1):77-78.
24. Anderlini P, Chan F, Champlin R, Körbling M, Strom S. Long-term follow-up of normal peripheral blood progenitor cell donors treated with filgrastim: no evidence of increased risk of leukemia development. *Bone Marrow Transplant*. 2002;30(10):661-663.
25. Socié G, Stone JV, Wingard JR, Weisdorf D, Henslee-Downey PJ, Bredeson C et al. Long-term survival and late deaths after allogeneic bone marrow transplantation: Late Effects Working Committee of the International Bone Marrow Transplant Registry. *N Engl J Med*. 1999;341(1):14-21.
26. Martin PJ, Counts Jr GW, Appelbaum FR, Lee SJ, Sanders JE, Deeg HJ et al. Life expectancy in patients surviving more than 5 years after hematopoietic cell transplantation. *J Clin Oncol*. 2010;28(6):1011-6.
27. Allan DS, Takach S, Smith S, Goldman M. Impact of declining fertility rates in Canada on donor options in blood and marrow transplantation. *Biol Blood and Marrow Transplant*. 2009;15(12):1634-7.