


ORIGINAL ARTICLE

Demand and usage of unrelated donor products for allogeneic haematopoietic cell transplantation during the COVID-19 pandemic: A Canadian Blood Services Stem Cell Registry analysis

David S. Allan^{1,2,3}  | Meagan Green¹ | Gail Morris¹ | Jason Weiss¹ |
Nicholas Dibdin¹ | Dena Mercer¹ | Matthew Seftel^{1,4}

¹Stem Cells, Canadian Blood Services, Ottawa, Ontario, Canada

²Clinical Epidemiology, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

³Department of Medicine and Biochemistry, Microbiology & Immunology, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

⁴Department of Medicine, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada

Correspondence

David S. Allan, The Ottawa Hospital, 501 Smyth Road, Box 704, Ottawa, ON K1H 8L6, Canada.

Email: daallan@toh.ca

Funding information

None declared.

Abstract

Background and Objectives: Understanding changes in the demand and usage of unrelated allogeneic haematopoietic cell transplantation (HCT) donors during the COVID-19 pandemic is needed to optimize pandemic preparedness of registry and donor collection services. The aim of this study was to understand the extent to which the pandemic has impacted the demand and usage of unrelated donors and cord blood units (CBUs) at Canadian Blood Services (CBS).

Materials and Methods: Data regarding stem cell donor interest and product usage for unrelated allogeneic HCT were retrieved from the database at CBS using de-identified anonymous information.

Results: Unrelated donor searches for Canadian patients remained unchanged by the pandemic, reflecting stable demand. The number of unrelated allogeneic transplants performed within Canada also remained stable, while the number of cord blood transplants increased, chiefly for paediatric patients. Requests for donor verification typing, a first signal of potential interest, increased from domestic centres during the first 6 months of the pandemic and decreased from international centres, before returning to baseline levels. The proportion of transplants for Canadian patients who used stem cell products procured from Canadian donors increased between 3 and 6 months after the start of the pandemic before returning to baseline and appears to be increasing again more than 1 year after the start of the pandemic. Use of CBUs for Canadian paediatric patients increased and remains elevated.

Conclusion: Demand for unrelated adult HCT donors has remained stable despite the evolving pandemic with a transient and recurring increased interest and usage of domestic adult donors. Use of CBUs for paediatric patients has increased and remains elevated. Registries and donor collection centres should maintain the capacity to expand services for domestic donor collection during pandemics to offset threats to international donor usage.

KEYWORDS

cord blood, COVID-19, donor usage, haematopoietic cell transplantation, pandemic, unrelated donor

Highlights

- Transient and recurring increased interest and usage of domestic donors for Canadian patients has occurred during the pandemic.
- Use of cord blood units from the Canadian Blood Services Cord Blood Bank has increased.
- Capacity for domestic donor evaluation and collection is needed during this pandemic to offset potential threats to international donor usage.

INTRODUCTION

COVID-19 has impacted the procurement of unrelated haematopoietic stem cells for allogeneic transplantation, and transplant centres have undergone significant changes in their approach to selecting donors for haematopoietic cell transplantation (HCT) [1, 2]. Aligning with many other countries [3], transplant centres in Canada initially deferred or delayed transplantation for some patients with non-urgent diagnoses to minimize the potential demand on intensive care units and to avoid hospital capacity crises. In many cases, however, deferring life-saving therapy was not possible, and many centres continued to perform HCT. Indeed, a recent report indicates greater mortality among patients whose transplants were delayed because of the pandemic [4]. Patients with aggressive leukaemias who could not be maintained with additional cycles of chemotherapy represented situations wherein the transplant could not be safely deferred. Moreover, recommendations from the World Marrow Donor Association [5], Cellular Therapy and Transplant Canada [6] and Canadian Blood Services (CBS) Stem Cell Registry [7] strongly encouraged transplant centres to cryopreserve all haematopoietic cell products prior to initiating the preparative regimen before transplant. This allowed the centres to continue with unrelated donor collections and defer the infusion of the cells until a later date, if necessary. Although the impact of the pandemic on adult registries and cord blood banks have been reported [8-10], the impact of COVID-19 on the demand and

usage of unrelated donors for Canadian centres has not been described. Given the regional differences in public health measures during the pandemic, understanding the changes in donor usage in Canada is important to optimize services that support patients and transplant centres as the pandemic evolves and to better prepare for possible future threats.

METHODS

Data were retrieved from the Stem Cell National System Solution, which houses prospectively collected data related to the management of donor searches in Canada (excluding the province of Quebec), the unrelated donor Stem Cell Registry, and the public Cord Blood Bank for CBS. Results were analysed in a before-and-after approach using descriptive statistics and considering 15 March 2020 as the initial date of the COVID-19 pandemic. All data were aggregated and anonymized before analysis.

RESULTS

Following the declaration of the global pandemic, new searches for unrelated donors from Canadian transplant centres remained comparable to levels before the pandemic (data not shown), suggesting

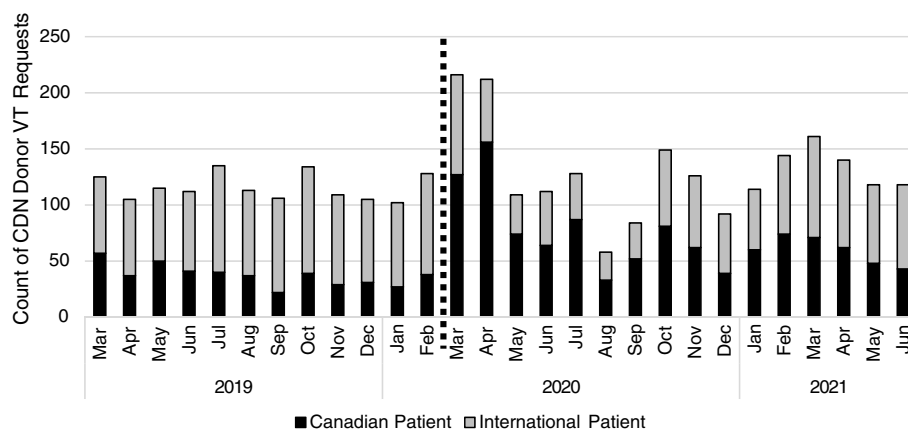


FIGURE 1 Efforts to identify donors on the Canadian Blood Services Stem Cell Registry by Canadian transplant centres, as reflected by increased requests for verification typing (VT), which increased during the initial 3–6 months after the start of the pandemic (black), with reduced requests from international centres (grey). Overall VT requests appeared to return to pre-pandemic levels approximately 6 months into the pandemic

stable demand for unrelated donors. Requests for verification typing (VT), which is the first step in potential donor selection and signals interest in potential donors, also remained stable with an increased proportion of VT requests arising from domestic transplant centres during the first 6 months of the pandemic and reduced levels of VT requests from international centres during the same time period (see

Figure 1). VT requests from Canadian and international centres returned to pre-pandemic levels by 6 months after the onset of the pandemic. Work-up requests for Canadian donors, whether initiated by Canadian or international transplant centres, remained stable in the first 6 months of the pandemic (14.8/month) compared to the 6-month period before the pandemic (13.2/month, $p = 0.48$). However, the proportion of Canadian donor work-ups for Canadian patients increased significantly during the first 6 months of the pandemic (29% before the pandemic vs. 52% post pandemic, respectively, $p = 0.003$). Moreover, collections occurred in a timely manner following the request to initiate a donor work-up. The mean number of days from work-up initiation to product collection over the 6 months before the pandemic was 45 days (range, 18–172) compared with 37 days (14–139) over the first 6 months of the pandemic. The total number of allogeneic transplants performed in Canada has remained stable at a mean rate of 33 unrelated donor transplants per month throughout the pandemic (data not shown). However, a greater proportion of transplants that used a domestic donor from the CBS Stem Cell Registry increased transiently between 3 and 6 months after the start of the pandemic, with decreased usage of international donors (see Figure 2). Usage of Canadian and international donors for Canadian patients returned to baseline levels after the 6-month mark

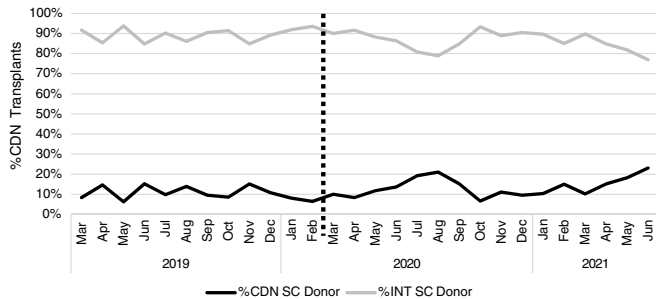


FIGURE 2 Proportional use of Canadian donors, as opposed to international donors, for Canadian patients, plotted over time. An apparent increase was observed for a brief period of several months starting from 3 months after the onset of the pandemic and may be increasing again in the most recent 3-month period

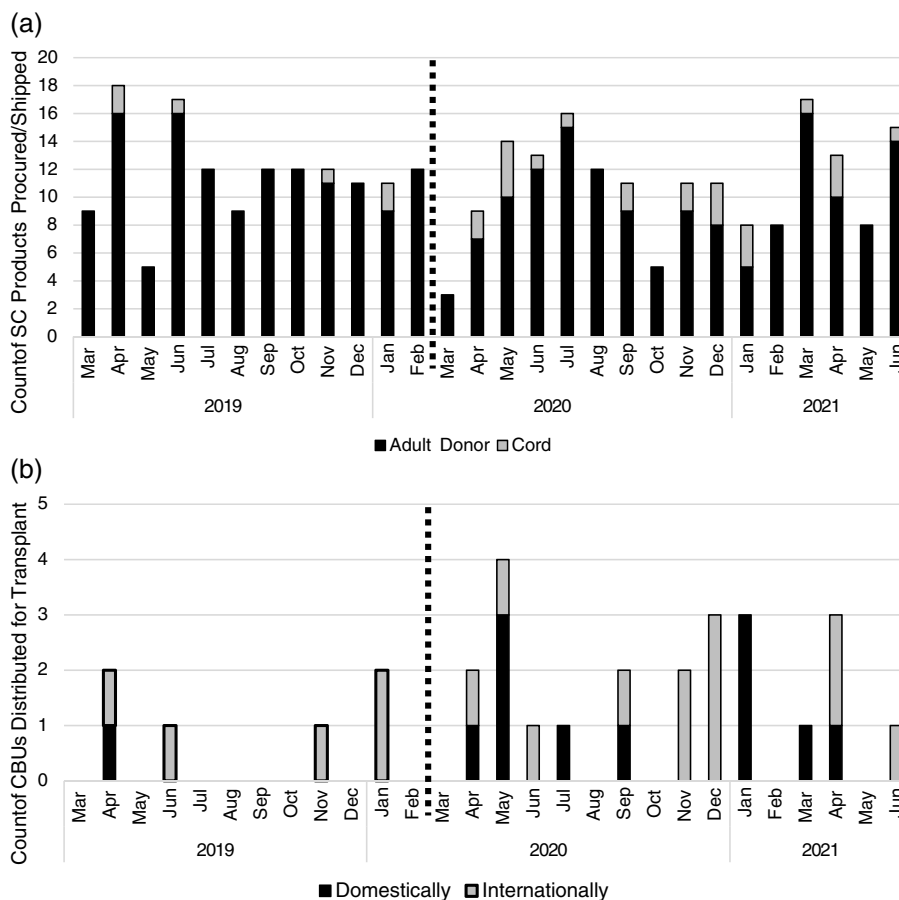


FIGURE 3 Usage of stem cell products from Canadian donors plotted over time. (a) Total number of unrelated donor products collected (black) and number of cord blood units (CBUs) distributed (grey) from Canadian donors. (b) CBUs distributed from the Canadian Blood Services cord blood bank over time to both Canadian (black) and international (grey) transplant centres

of the pandemic but may be increasing again in the second quarter of 2021 (see Figure 3).

Regarding the procurement of stem cell products from Canadian donors, we observed stable rates of donor collections after the onset of the pandemic compared to pre-pandemic levels (see Figure 3a), except for the first month of the pandemic. The use of cord blood units (CBUs) from the CBS's Cord Blood Bank for domestic transplant centres (exclusively for paediatric patients) has increased and remained elevated compared to baseline levels (see Figure 3b).

In response to the recommendations from national and international bodies, the majority of products collected from unrelated donors have been cryopreserved (68% of products collected from Canadian donors from March 2020 to June 2021) before infusion in comparison to 4% in the 12 months before the pandemic and approximately 7% noted in a historical cohort that was previously described [11]. With regard to adverse events related to cryopreservation, none of eight adverse event reports that were filed by CBS to the World Marrow Donor Association between January 2019 and March 2020 was related to cryopreservation, whereas between March 2020 and June 2021, a total of four adverse events were reported, all of which described impacts related to cryopreservation.

DISCUSSION

Transplant centres in Canada have continued to search for unrelated donors and CBUs for their patients during the COVID-19 pandemic. A shift to increased interest in donors from the CBS Stem Cell Registry and a significant increase in usage of units from the CBS's Cord Blood Bank have occurred, likely reflecting perceived advantages in the availability of domestic donors/CBUs and simplified logistics related to the transportation of a product procured within the country. Cryopreservation of adult unrelated donor products during the first 6 months and beyond by Canadian transplant centres was used to mitigate against potential unforeseen logistical barriers and scheduling challenges related to the pandemic. These data support the substantial value to HCT centres and their patients of maintaining a national registry of adult unrelated donors and a public inventory of high-quality CBUs during this pandemic.

Although the continued demand for new searches for adult unrelated donors highlights the ongoing needs of patients despite the pandemic, it underscores the perceived importance of human leucocyte antigen (HLA) matching on patient outcomes. Other recent reports outline the steps taken by adult registries to meet the ongoing demand for unrelated donors during the pandemic and describe a reduction in the use of bone marrow, an increased usage of domestic donors, more work-up requests in case backup donations were needed, and more donor cancellations attributed to COVID-19 [8, 9]. The increased focus on domestic donors reflects considerations related to constraints on donor travel to hospitals, collection centre staff, courier arrangements, and cryopreservation requirements. In

cases where multiple potential donors were identified from the CBS Stem Cell Registry, information regarding donor proximity to donor centres was provided to transplant centres as a means of reducing risks related to donor travel. While it is possible that unrelated donor products may be collected, cryopreserved, and then stored until a time when transplants can be safely scheduled, most transplants occurred within a short time after cryopreservation was completed. Adverse events related to cryopreservation were uncommon, but did occur. Taken together, this highlights the balance between the advantages of cryopreservation and potential negative issues related to the process of cryopreservation and its impact on transplantation outcomes as well as the risk that cryopreserved products may pose [12–15].

The ability to continue with unrelated donor collections during this pandemic reflects the urgent nature of many transplants and the high level of commitment of donors and collection centres to the process of donation. Interest and usage of CBUs from the CBS bank increased substantially, likely reflecting interest in a product that was collected before the pandemic and which is already stored and ready for distribution without the need for a personal courier. Transplant centres may have preferred to organize transplants using cord blood given the increased certainties associated with delivery and scheduling and the predictable high quality of the units [16]. A 7% increase in the usage of CBUs was reported by one European network of banks while banking efforts were stalled during the early stages of the pandemic [10].

Although new collections and banking of CBUs and registration of potential donors at in-person swabbing events were halted during the initial stages of the pandemic, resuming these activities carries increased urgency given our observations of increasing demand. With adaptations to the pandemic, collection and banking of CBUs resumed in Canada within a period of 4 months. Shifting the registration of potential donors to a completely on-line registration process has occurred, which may enhance donor availability at the time of donor activation [17]; however, the effectiveness of this method remains a challenge.

Unrelated donor registries will need to continue to track the trends and challenges related to the ongoing COVID-19 pandemic in order to ensure continued access to high-quality CBUs and unrelated donor products within Canada and abroad. In addition, registries will need to ensure that relevant services such as donor collection facilities and cryopreservation services at cell processing labs remain safely available.

ACKNOWLEDGEMENTS

D.S.A. conceived the study design. M.G., G.M., and J.W. performed data extraction and data analysis. D.S.A. and M.S. were responsible for the initial drafting of the manuscript. All authors were involved in manuscript revisions before final approval.

CONFLICT OF INTEREST

All authors are employed and/or paid consultants at Canadian Blood Services. There are no other conflicts of interest.

ORCID

David S. Allan  <https://orcid.org/0000-0003-3261-8289>

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How to cite this article: Allan DS, Green M, Morris G, Weiss J, Dibdin N, Mercer D, et al. Demand and usage of unrelated donor products for allogeneic haematopoietic cell transplantation during the COVID-19 pandemic: A Canadian Blood Services Stem Cell Registry analysis. *Vox Sang.* 2022.