Health-Related Quality of Life among Pediatric Hematopoietic Stem Cell Donors

Galen E. Switzer, PhD[1,2,3,4], Jessica Bruce, BA[2], Deidre M. Kiefer, MPH[5], Hati Kobusingye, MS[5], Rebecca Drexler, BS, AAS[5], RaeAnne M. Besser, BS[5], Dennis L. Confer, MD[5], Mary M. Horowitz, MD, MS[6], Roberta J. King, MPH[5], Bronwen E. Shaw, MD, PhD[6], Suzanna M. van Walraven, MPA, PhD[7,8], Lori Wiener, PhD[9], Wendy Packman, PhD, JD[10], James W. Varni, PhD[11,12], and Michael A. Pulsipher, MD[13]

Objectives To examine health-related quality of life (HRQoL) among sibling pediatric hematopoietic stem cell donors from predonation through 1 year postdonation, to compare donor-reported HRQoL scores with proxy-reports by parents/guardians and those of healthy norms, and to identify predonation factors (including donor age) potentially associated with postdonation HRQoL, to better understand the physical and psychosocial effects of pediatric hematopoietic stem cell donation.

Study design A random sample of 105 pediatric donors from US centers and a parent/guardian were interviewed by telephone predonation and 4 weeks and 1 year postdonation. The interview included sociodemographic, psychosocial, and HRQoL items. A sample of healthy controls matched to donors by age, gender, and race/ethnicity was generated.

Results Key findings included (1) approximately 20% of donors at each time point had very poor HRQoL; (2) child self-reported HRQoL was significantly lower than parent proxy-reported HRQoL at all 3 time points and significantly lower than that of norms at predonation and 4 weeks postdonation; and (3) younger children were at particular risk of poor HRQoL.

Conclusions Additional research to identify the specific sources of poorer HRQoL among at-risk donors (eg, the donation experience vs having a chronically ill sibling) and the reasons that parents may be overestimating HRQoL in their donor children is critical and should lead to interventions and policy changes that ensure positive experiences for these minor donors. *(J Pediatr 2016;178:164-70).*

See editorial, p 14

During the past 50 years, allogeneic hematopoietic stem cell (HSC) transplantation has become a preferred treatment for multiple blood and immune-related disorders.[1] Allogeneic HSC donation involves removing stem cells from a healthy donor, in this case a sibling child, through either a surgical bone marrow collection or a peripheral blood stem cell (PBSC) procedure, and infusion of these cells into the ill sibling recipient.[2] In 2013, there were 1578 US pediatric HSC transplants, and the number of pediatric HSC transplants has been increasing yearly.[3] Although the use of minors as HSC donors is considered medically safe[4] and legally accepted given that no alternative approach of comparable effectiveness exists, policy statements by the American Academy of Pediatrics[5] and published reviews of the literature cite a lack of understanding of the physical and psychosocial effects of pediatric HSC donation and call for investigations of such effects.[6-8]

Published reviews identified only a handful of studies of health-related quality of life (HRQoL) in sibling pediatric HSC donation.[6,7] Authors of these reviews and other published investigations conclude that there is a critical need to better understand the donation-related experiences of this group.[8-11] The few published find-

HRQoL	Health-related quality of life
HSC	Hematopoietic stem cell
PBSC	Peripheral blood stem cell
PedsQL	Pediatric Quality of Life Inventory

From the [1]Departments of Medicine, University of Pittsburgh, Pittsburgh, PA; [2]Psychiatry, University of Pittsburgh, Pittsburgh, PA; [3]Clinical and Translational Science, University of Pittsburgh, Pittsburgh, PA; [4]Center for Health Equity Research and Promotion, Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA; [5]Center for International Blood and Marrow Transplant Research, National Marrow Donor Program/Be The Match, Minneapolis, MN; [6]Center for International Blood and Marrow Transplant Research, Department of Medicine, Medical College of Wisconsin, Milwaukee, WI; [7]Sanquin Blood Supply, Department of Donor Services, Amsterdam, The Netherlands; [8]Willem Alexander Children's Hospital, Department for Pediatric Stem Cell Transplantation, Leiden University Medical Center, Leiden, The Netherlands; [9]Center for Cancer Research, National Cancer Institute, Bethesda, MD; [10]Department of Psychology, Palo Alto University, Palo Alto, CA; [11]Department of Pediatrics, Texas A&M University, College Station, TX; [12]Department of Landscape Architecture and Urban Planning, Center for Health Systems and Design, Texas A&M University, College Station, TX; and [13]Division of Hematology, Oncology, and Bone Marrow Transplantation, Children's Hospital Los Angeles, Los Angeles, CA

Supported by the National Heart, Lung, and Blood Institute (R01 HL085707). J.V. holds the copyright and the trademark for the Pediatric Quality of Life Inventory and receives financial compensation from the Mapi Research Trust, which is a nonprofit research institute that charges distribution fees to for-profit companies that use the Pediatric Quality of Life Inventory. The other authors declare no conflicts of interest.

0022-3476/$ - see front matter. Published by Elsevier Inc.
http://dx.doi.org10.1016/j.jpeds.2016.07.009

ings suggest that pediatric donors may experience psychosocial issues around the time of and following donation including higher anxiety and lower self-esteem than nondonors,[12] moderate levels of posttraumatic stress, depression, behavioral problems, identity problems, guilt, and resentment.[7,12,13] Young donors may also fear the medical aspects and pain involved in donation and experience anxiety and ambivalence about donation.[14,15] Following donation, 25%-35% of donors and their families have expressed a need for more predonation information about the donation process.[8,16] Although there is evidence of the potential HRQoL risks associated with pediatric HSC donation, the investigations providing this evidence have limitations including descriptive cross-sectional designs, small, nonrepresentative samples, varying time of posttransplant data collection, and lack of child self-reported HRQOL.[6,7]

The current investigation of sibling pediatric donors was part of a larger study focused on the medical safety and HRQoL of related HSC donation. In addition to large samples of related and unrelated adult HSC donors, the parent study included a smaller sample of sibling pediatric donors. The goals of the pediatric HRQoL substudy were to (1) longitudinally examine HRQoL among sibling pediatric HSC donors from predonation through 1 year postdonation and to compare donor child self-reported scores with parent/guardian proxy-reported scores and normative sample HRQoL scores; (2) examine the potential association of donor age with HRQoL; and (3) determine which predonation factors were most strongly associated with donor child HRQoL at 4 weeks and 1 year postdonation.

Methods

This investigation was approved by the Institutional Review Boards at the University of Pittsburgh, the National Marrow Donor Program, and participating transplant centers. All parents signed informed consent and children gave assent before completing interviews.

Donors and Their Parents/Guardians

This investigation included sibling pediatric HSC donors ages 5-18 years from 24 transplant centers enrolled in the parent Multi-Institutional Study of HSC Donor Safety and Quality Life investigation (ClinicalTrials.gov: NCT00948636) who donated bone marrow or PBSC in the US between April 2010 and May 2013 and 1 of their parents/guardians.

Potential participants were required to meet the standard requirements for donation, be first-time donors, and assent/consent to participate in both the parent Multi-Institutional Study of HSC Donor Safety and Quality Life and the donor HRQoL substudy. Potential participants were excluded if they did not speak English, were unable to complete a telephone interview because of cognitive or linguistic difficulties, or had no access to a telephone as determined by the transplant centers interacting with them.

Individual transplant centers consented participants for the study and passed contact information of enrolled donors to University of Pittsburgh staff. Parent-child pairs who consented entered the random selection pool for the HRQoL substudy with a target sample goal of 100. Interviewers from the University of Pittsburgh contacted participants by telephone within 4 weeks prior to bone marrow donation, or 4 weeks prior to initiation of granulocyte colony stimulating factor administration, to complete a baseline interview. All donors were interviewed again at 4 weeks and 1 year after donation. The interviews required approximately 20 minutes to complete.

Healthy Normative Sample

A normative sample of 537 healthy children matched to the donor sample by age, sex, and race/ethnicity was generated from existing data and provided for this work by the developer of the Pediatric Quality of Life Inventory (PedsQL). Norm-based guidelines for the PedsQL are also available as derived from existing sample of >9500 healthy children assessed during the PedsQL validation phases.[17-19]

Study Measures

Three categories of participant characteristics were assessed by HRQoL (primary outcome), sociodemographic, and psychosocial characteristics. Measures were previously validated scales/items with established measurement properties either created for, or used in, other donation-related settings. Recipient status at 1 year following donation was collected directly from transplant center records.

HRQoL

HRQoL was assessed with the PedsQL 4.0 Generic Core Scales comprising 23 items assessing functioning in the past month across 4 dimensions: physical (8 items), emotional (5 items), social (5 items), and school (5 items).[17-19] Age appropriate-validated versions of the PedsQL were administered. The parent version of the PedsQL asks the same questions as the child version. Parents and children completed the interviews independent of one another. Following standard procedures, responses were transformed to a 0-100 score with a higher score indicating better HRQoL. Responses from the emotional, social, and school functioning scales comprised the psychosocial health summary score. All items combine to produce a total HRQoL score. In addition to a total score, an "at risk" cut-off score of ≤69.71 has been suggested by the PedsQL developers.[19] Children scoring at or below this cut-off have HRQoL similar to that of chronically ill children.[18,19]

Sociodemographic Characteristics

Donor, recipient, and parent/family sociodemographic characteristics were gathered from parents/guardians and included (1) donor age, sex, race/ethnicity, and relationship to the recipient, (2) recipient age and sex, and (3) parent/guardian relationship to the donor, age, education level, relationship status, number of children, and family income. For most analyses, donor age was converted to a categorical variable corresponding to the developmental age categories defined by the PedsQL.[17] These age categories are 5-7 years, 8-12 years, and 13-18 years, and age appropriate but statistically comparable versions of the PedsQL are administered to these groups. Donors were assigned to an age group based on their age at