Practice patterns for evaluation, consent and care of related donors and recipients at hematopoietic cell transplant centers in the United States

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Running heads:

Left: O’DONNELL et al

Right: SURVEY OF DONOR PRACTICE PATTERNS IN THE US
ABSTRACT

A conflict-of-interest may arise when a single physician serves two individuals whose medical care is interdependent. In hematopoietic cell transplantation (HCT) from unrelated donors and in the setting of solid organ transplantation from living donors, the standard-of-care is for donors and recipients to be managed by separate physicians in order to provide unbiased care. However, the practice patterns of evaluation and care of related donors and recipients are not well described. A survey of HCT centers in the United States was conducted by the Donor Health and Safety Working Committee of the CIBMTR to determine the type of provider involved in medical clearance, informed consent and medical management of hematopoietic cell collection, and the relationship of that provider to the HCT recipient. The response rate was 40%. In greater than 70% of centers, transplant physicians were involved or potentially involved in overlapping care of the HCT donor and the recipient. These patterns were similar between transplant teams caring for adult or pediatric donors and recipients. Among responding centers, medical management of recipients and their related donors by the same provider is common, a practice which has the potential for conflict-of-interest.
INTRODUCTION

Foster\(^1\) has written eloquently about conflict of interest that can arise in a clinical setting when a subtle bias of a physician may unknowingly affect their sound judgment in caring for a vulnerable individual. Trust placed in the physician by a patient may be jeopardized by such physician bias, real or perceived. In each allogeneic HCT, there are two patients; one is the transplant recipient for whom the procedure may be life-saving and the other is the donor, who may have nothing medically to gain from the donation procedure. When the donor and the recipient are relatives, most often siblings in HCT, unique issues arise concerning medical risks, familial responsibilities, emotional burdens, and privacy. These issues may be further complicated if a single physician has overlapping care responsibilities for both the donor and recipient. For example, a prospective donor being evaluated by their sibling’s transplant physician may feel disinclined to admit their own reluctance or their fears of donation given the enormity of the sibling’s medical issues. Or, if these issues are broached, they may be underevaluated by the physician who is committed to completing the sibling’s transplant, and who may see no alternatives for the donor. At another extreme, a highly committed donor and transplant physician may collaborate to gloss over medical issues that create significant donor risk.

In the evaluation and care of unrelated hematopoietic cell donors, the situation regarding potential conflict-of-interest is clear. Both standard 9.3313 of the National Marrow Donor Program (NMDP)\(^2\) and standard 6.07 of the World Marrow Donor Association (WMDA)\(^3\) state that the medical evaluation of the unrelated donor must be performed by a physician who is not a
member of the transplant team that is caring for the patient. A similar guideline applies to related or unrelated solid organ donation. While most U.S. HCT centers are accredited by the Foundation for the Accreditation of Cellular Therapy (FACT), the issue of whether the donor and recipient care should be managed by distinctly separate providers is not addressed explicitly by FACT-JACIE Standards.

The practice patterns of evaluation and care of related donors and recipients at centers performing allogeneic HCT currently are not well described. We hypothesized that overlapping care of HCT related donors and recipients by a single physician may be common practice in the U.S. If true, this would create the opportunity to educate HCT teams on the potential risks of such practices and to develop strategies for mitigating those risks. To address our hypothesis we surveyed U.S. transplant centers within the CIBMTR to determine how closely existing practice patterns for related donors followed the donor safety guidelines of the NMDP, WMDA, or of the solid organ transplant field.

METHODS

Subjects

A total of 265 medical directors representing 222 transplant teams received invitations to participate in the survey between December 2007 and July 2008. A total of 239 medical directors were identified from the CIBMTR transplant teams, and an additional group of 35 medical directors were also invited from teams participating in the Children’s Oncology Group. Centers were grouped according to their geographic location in the analysis. U.S. regions included: New England (ME, NH, VT, MA, RI, CT); Mid-Atlantic (NY, NJ, PA); South Atlantic
(DE, MD, DC, VA, WV, NC, SC, GA, FL); East North Central (OH, IN, IL, MI, WI); East South Central (KY, TN, AL, MS); West North Central (MN, IA, MO, ND, SD, NE, KS); West South Central (AR, LA, OK, TX); Mountain (MT, ID, WY, CO, NM, AZ, UT, NV); Pacific (WA, OR, CA, AK, HI).

Survey Instrument

An internet-based survey questionnaire (Appendix) was created and administered through a secure hyperlink (www.surveymonkey.com). The survey’s objectives were (i) to determine the type of provider involved in three different aspects of donor care: medical clearance, informed consent and medical management of hematopoietic cell collection, and (ii) to determine the relationship of that provider to the HCT recipient. The types of providers identified were those associated with the transplant team (transplant physician, mid-level practitioner or nurse) and those not associated with the transplant team (internal/family medicine physician, hematology/oncology physician or pediatrician). Donor medical clearance is the process of determining that the donor is medically fit for donation of bone marrow or peripheral blood stem cells, as well as identifying any risks that donor cells might pose for the intended recipient, e.g., infectious disease transmission. Medical management of the donor cell collection concerns the actual donation process, management of donation-related adverse events and donor follow-up. Six invitations to participate in the survey were sent, and an incentive to participate was offered to increase the response rate. All procedures were approved by the CIBMTR IRB. See Appendix for tabulation of survey data.
RESULTS

Response rate

A total of 115 responses were received. Excluding 3 responses from centers that did not perform allogeneic transplants and 14 duplicate responses, there were 98 evaluable responses from 88 transplant programs, which resulted in a response rate of 40%.

Center Characteristics

Characteristics of responding centers are shown in Table 1. About half of the centers performed transplants for both adult and pediatric patients. The remaining centers were divided equally between centers transplanting only adults or only children. The combined programs performed significantly more transplants from related donors than programs transplanting only adults or only children. Most centers were FACT-accredited and also were transplant centers affiliated with the NMDP. Almost all centers had a written policy for management of related donors.

Responding vs. Non-responding centers

Figure 1 compares characteristics of those centers who responded to the survey, and those who did not. Responding centers were distributed across the center-size spectrum, while nearly 70% of non-responding centers were from those performing fewer than 30 transplants per year. (Panel A). There were no differences in the geographical distribution of responding and non-responding centers (Panel B).
Providers involved in donor care

Figure 2 shows the role of the provider in the care of donors. Panel A shows that in ≥80% of centers surveyed, a transplant physician was involved in the medical clearance, obtaining informed consent and/or medical management of the donor. Panel B shows that in >70% of centers surveyed, the same physician caring for the donor had either simultaneous responsibility for the care of the recipient or might be involved in the care of the recipient.

Center volume effect

Figure 3 shows the effect of center volume on the role of the physician caring for the donor in the care of the recipient. Panel A shows that in >75% of centers surveyed where the total transplant volume was <100 per year the physician responsible for medical clearance of the donor also had either simultaneous responsibility for the care of the recipient or might be involved in the care of the recipient. In transplant centers performing ≥100 transplants per year there tended to be less involvement of the donor’s attending physician in care of the recipient. In centers performing 100-299 transplants per year, 30% responded that the donor’s physician was affiliated with the transplant center but not involved in the care of the recipient. This number increased to 50% in centers performing ≥300 transplants per year. Panel B shows similar results for the physician responsible for the medical management of the donor. However, in about 20-30% of large transplant centers (≥100 transplants per year) the donor’s physician also had simultaneous responsibility for care of the recipient. The process of informed consent also followed the same practice pattern (data not shown).
DISCUSSION

Transplant center directors in the US were surveyed by the Donor Health and Safety Working Committee of the CIBMTR to determine the practice patterns of evaluation and care of related donors and recipients, practice patterns which had not been assessed previously. Although there was no difference in geographical distribution of responding and non-responding centers, almost 70% of non-responding centers were small centers performing $\leq 30$ transplants per year. Of some concern was the finding that a few transplant centers (5%) did not have written policies for management of related donors. Not surprisingly, $\geq 80\%$ of related donors in responding centers received care by physicians whose primary role was the care of patients undergoing HCT. However, we found that in $> 70\%$ of responding centers, physicians who were involved in the care of the recipient also were apt to be involved in the medical clearance, informed consent and medical management of the recipient’s donor. There was an effect of center size since direct involvement of the same physician in both the recipient’s and donor’s care occurred less frequently in centers performing $\geq 100$ transplants per year. Since the same physician was more likely to be involved in the care of both donor and recipient at small centers our survey results may actually underestimate the extent of the prevalent practice pattern we observed. However, the survey response rate was only 40% so it is difficult to generalize our results to the entire transplant community. Staffing issues could be one explanation for the observed center effect in smaller transplant centers where the number of transplant physicians available for independent donor care may be limited. Contrary to the prevalent practice, specific transplant expertise may not be required to perform evaluation, consent and management of donors. Thus, where staffing is problematic, uninvolved providers, e.g., internists, pediatricians or physician extenders with
the appropriate expertise could be utilized who would not necessarily need to be in the same practice location. Non-transplant providers could easily be trained to understand relevant transplantation and donation issues. An independent provider and advocate could be especially important in the case of pediatric donors where there is an inherent conflict-of-interest in the decision-making of the consenting parent.

The findings of our survey suggest that there exists a potential for physician conflict-of-interest in the management of related HCT donors at a substantial number of transplant centers in the US. Although actual conflicts-of-interest may occur infrequently, these findings are concerning because a potential or perceived conflict-of-interest could be as damaging as an actual conflict-of-interest by jeopardizing trust in the physician. This potential may be even more significant, since the related donors themselves may be willing participants who knowingly (or not) obscure or ignore medical concerns that could preclude donation. There is no direct medical benefit to the stem cell donor other than the possible diagnosis of an unrecognized medical problem discovered during evaluation so the potential for biased decision-making by a conflicted physician could result in harm, especially to the increasing number of older donors who may have significant co-morbid conditions.

Several possible assumptions about related donors made by the transplant community could explain the reported practice patterns. One is that care of related donors and recipients is not interdependent which may obviate a concerted effort by transplant centers to have an uninvolved provider assume care of the donor. Another is that hematopoietic cell donation is ordinarily a low-risk procedure, akin to blood or platelet donation, and conceptually different from solid
organ donation. An unsubstantiated assumption is that related donors are willing to accept greater risks because of the positive emotional benefit they receive by the knowledge of helping a family member with a life-threatening illness. While it may be acceptable for a related donor to accept greater risk in the donation process, disclosure of such risks should be delivered by a provider without bias or perception of bias by involvement with the recipient’s care. However, one must also consider the possibility of negative emotions such as feelings of coercion, anxiety, anger, and guilt, especially if the transplant were not successful or if there were serious transplant-related complications. There are limited studies of psychological risks to related donors with small numbers of subjects, especially adult donors. A common experience of both pediatric and adult donors in these studies was the feeling that their needs and concerns were subservient to those of the recipient. It is possible that the prevalent practice of care of related donors and recipients by the same physician shown by our survey might contribute to such negative feelings held by donors. There are no studies addressing the psychological consequences of being found an unsuitable donor. Physical and psychological issues may be difficult to address during the evaluation, consent and management phases of donor care if the physician is perceived as focused primarily on the care of the recipient.

Given the highly prevalent practice pattern of donor care shown by this study, we encourage the transplant community to conduct a careful review of their donor practice patterns and consider taking the necessary steps to minimize, and preferably eliminate, the potential for conflict-of-interest. For example, the guidance for the FACT Standards, 4th edition was revised recently to recommend involvement of an independent physician in donor care similar to a recent recommendation by the WMDA. We feel that it is time for an explicit FACT-JACIE standard
to this effect. HCT donors and their recipients are likely to be served best by receiving all aspects of their care from different physicians whose fiduciary responsibility is to only one individual as is required by the NMDP and WMDA for unrelated donors and by the solid organ transplantation field.
Authorship

PVO and DLC supervised the project. PVO, TLP, DLC, JDR, MP, SL and PA designed the survey. PVO drafted the manuscript with critical review provided by DLC, JDR, MP, DS, SL, and PA. TLP provided statistical analyses. The authors have no conflict of interest to disclose.

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REFERENCES


## Table 1. Characteristics of responding centers.

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<th>Pediatric only</th>
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<td>56</td>
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<td>Institutional Characteristics</td>
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<td>Related donor transplants per year, median (range)</td>
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<td>25 (1-400)</td>
<td>10 (3-60)</td>
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<td>Related donor transplants per year</td>
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<td></td>
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<td>&lt;10</td>
<td>8 (38)</td>
<td>18 (32)</td>
<td>13 (62)</td>
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<td>11-40</td>
<td>11 (52)</td>
<td>24 (43)</td>
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<td>41-70</td>
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<td>5 (9)</td>
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<td>71+</td>
<td>2 (10)</td>
<td>9 (16)</td>
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<td>Total transplants per year, median (range)</td>
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<td>90 (5-600)</td>
<td>40 (10-270)</td>
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<td>Total transplants per year</td>
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<td>&lt;30</td>
<td>3 (14)</td>
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<td>22 (39)</td>
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<td>300+</td>
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<td>FACT-accredited center</td>
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<td>Written policy for related donor management</td>
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<td>52 (93)</td>
<td>21 (100)</td>
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Figure 1. Characteristics of responding and non-responding centers.

Panel A: Distribution of transplant volumes at responding and non-responding centers.

Panel B: Geographic distribution of responding and non-responding centers. U.S. regions: NEng, New England; Mid-Atl, Mid-Atlantic; So-Atl, South Atlantic; ENC, East North Central; ESC, East South Central; WNC, West North Central; WSC, West South Central; Mt, Mountain; Pac, Pacific.
Figure 2. Provider responsible for donor care.

Panel A: Providers associated with the transplant team (transplant physician, mid-level practitioner or nurse); providers not associated with the transplant team (internal/family medicine physician, hematology/oncology physician or pediatrician).

Panel B: Involvement of donor’s provider in care of the recipient.
Figure 3. Effect of center volume on donor care patterns.

Panel A: Role of provider responsible for donor medical clearance in care of recipient.

Panel B: Role of provider managing donor medical care in care of recipient.
Practice patterns for evaluation, consent and care of related donors and recipients at hematopoietic cell transplant centers in the United States