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Considering tangible benefit for interdependent donors: Extending a risk-benefit framework in donor selection

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Abstract

From its infancy, live donor transplantation has operated within a framework of acceptable risk to donors. Such a framework presumes that risks of living donation are experienced by the donor while all benefits are realized by the recipient, creating an inequitable distribution that demands minimization of donor risk. We suggest that this risk-tolerance framework ignores tangible benefits to donor. A previously proposed framework more fully considers potential benefits to the donor and argues that risks and benefits must be balanced. We expand on this approach, and posit that donors sharing a household with and/or caring for a potential transplant patient may realize tangible benefits that are absent in a more distantly related donation (e.g. cousin, non-directed). We term these donors, whose wellbeing is closely tied to their recipient, "interdependent donors." A flexible risk-benefit model that combines risk assessment with benefits to interdependent donors will contribute to donor evaluation and selection that more accurately reflects what is at stake for donors. In so doing, a risk-benefit framework may allow some donors to accept greater risk in donation decisions.

When accepting the Nobel Prize in Physiology or Medicine in 1990 for his contribution to organ transplantation, Dr. Joseph Murray stated, "For the first time in medical history a normal healthy person was to subjected to a major surgical operation not for his own benefit." From its outset, the transplant community has dismissed any potential benefits to the donor in live donor transplantation. The problem of risk-benefit distribution, in which the donor accepts physical risk so that the recipient can realize the benefit of a transplanted

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SUPPORTING INFORMATION
The qualitative data presented in this study were collected as part of a pilot of an ongoing longitudinal study of partners and spouses of transplant candidates and recipients. We conducted semi-structured in-depth interviews with 4 partners or spouses of transplant candidates and 2 partners or spouses of transplant recipients from February to April 2016. Participants were asked about changes in quality of life, caregiving burden, marital quality, employment and economic situations, and personal plans as their spouse or partner initiated dialysis or received a transplant. Interviews were recorded, transcribed and thematically coded using NVivo. This study received human subjects research approval from the Johns Hopkins Medicine Institutional Review Board [IRB00084611].

organ, has been a core ethical problem for transplantation, and this inequitable distribution has been mitigated by minimizing risk to living donors. However, this conceptual approach has led the transplant community to base its assessment and selection of donors in a framework that identifies acceptable levels of risk to donors, and excludes consideration of any potential benefit to donors other than emotional or psychosocial.

The deceased donor organ supply is inadequate for the growing kidney transplant (KT) needs in the United States. With over 100,000 end-stage renal disease (ESRD) patients currently on the waitlist for a deceased donor kidney, live kidney donation (LKD) offers ESRD patients a timely treatment modality that has superior outcomes to deceased donor transplantation and hemodialysis. Improving access and removing disincentives to LKD is a strategic priority of the Organ Procurement and Transplantation Network (OPTN) and the United Network for Organ Sharing (UNOS).

We are in an era where donor evaluation and selection is based on clinical assessment of acceptable risk. The recent Kidney Disease Improving Global Outcomes (KDIGO) guideline on live kidney donor candidate evaluation promotes the use of quantitative, evidence based data to determine acceptable levels of risk to donors (1). Previously, Allen, Abt and Reese proposed that benefits to potential donors should be considered in donor evaluation, questioning a long-standing assumption that benefits from LKD flow only to the recipient, while the donor experiences only risk from donation (2). KDIGO guidelines further call for the assessment of “donor candidate benefits” during donor evaluation. New attention to donor benefit is a move towards more fully describing the realities of donor and recipient experiences and, with that, requires a novel shift from the existing framework of assessing acceptable risk toward one of a fuller balancing of both risk and benefit.

We describe the current risk evaluation and donor selection framework in LKD, including recently discussed donor-centered modifications and the recent movement toward consideration of benefits to donors (2, 3). We propose an expanded framework of balancing risks and benefits that focuses on the interdependency of many donor-recipient relationships, and more fully accounts for tangible benefits realized by donors. In addition, we suggest a research agenda to empirically assess donor benefit from LKD and how these benefits relate to donor-recipient relationships. Thus, we argue that when assessing and selecting potential living donors, risks to living donors must be balanced with both the donor’s willingness to accept risk and an empirical assessment of potential benefits to the donor. We further argue that potential benefits of donation may be greater for donors in close, interdependent relationships with their recipients, and that these relationships should factor into the balancing of risks and benefits during donor assessment and selection.

CURRENT FRAMEWORK OF ASSESSING ACCEPTABLE RISK IN LKD EVALUATION

In some respects, the current framework of assessing acceptable risk to donors is similar to the ethics framework underpinning approaches to research involving human subjects (4–7). All research involves uncertainty regarding the potential harms and potential benefits of participation, and in early phase trials participants assume risk with little if any possibility of direct benefits to them. Rather, participants assume risk knowing that most if not all benefits will flow to future patients and to society. Likewise, LKD requires the donor to assume risk, and in current approaches of assessing acceptable risk, it is presumed that benefits flow only to the transplant recipient (8).

In the predominant model of donor evaluation and selection, ethically acceptable transplants require minimizing risk to the donor and low levels of acceptable risk. However, clinical practice varies and there is not consensus on the maximum acceptable risk level. (3). In clinical practice, transplant centers often pre-define an acceptable risk (for example, a BMI cutoff), which then prevents any shared decision-making with the potential donor. When a potential donor is willing to accept greater risk than is the transplant center, the individual is prevented from donation. The refusal or rejection of a donor represents a wrong to that individual in denying their autonomous decision to donate (2).

BROADENING THE FOCUS FROM ACCEPTABLE RISK TO BALANCING RISKS AND BENEFITS

Recognizing transplant center variability and in response to the movement toward patient-centered healthcare, Thiessen et al. recently argued for a donor-centered modification to the framework focused on acceptable risk, offering a “principled way to redefine the range of potential benefits to the donor that are taken into account during the evaluation process (3).” Thiessen et al. focus particularly on the “discretionary donor” – medically complex donors who are willing to accept a higher level of risk than their transplant center will currently allow. A donor-centered approach, as Thiessen et al. describe, would allow the potential donor to become engaged in the evaluation and decision-making process. By balancing obligations to avoid causing harm with respect for patient autonomy, such an approach is certainly an improvement over the typical acceptable risk framework; the participation of potential donors represents some progress toward better capturing personal motivations for donation. However, even such a donor-centered approach is primarily concerned with finding shared perceptions of acceptable risk between the donor and the center and does not directly address tangible benefits that donors expect.

Allen, Abt and Reese propose the novel approach of considering the risks of turning down potential donors who would benefit from donation (2). This consideration broadens and more fully captures the donor experience and thereby improves donor decision making and the informed consent process. Furthermore, their approach draws attention to the limited focus on potential benefits to donors, and call for a more thorough understanding of what those benefits may be.

Like Allen, Abt and Reese, we advocate for a departure from a sole focus on acceptable risk to donors towards a framework that more fully assesses and balances potential benefits to donors with the risks. We expand their approach by considering the interests of donors who may experience tangible benefits from donation as part of the risk assessment. Under our framework, donors likely to experience greater tangible benefits (more benefits or more significant benefit than under evaluation and selection approaches not taking such benefits into account) might be permitted to donate when previously their risk profile would have been beyond a center's thresholds of acceptable risk. The shift in conceptual emphasis between the two donor evaluation and selection frameworks is further described below.

EXPANDING THE SPECTRUM OF TANGIBLE DONOR BENEFITS

A risk-benefit balance approach to donor evaluation and selection should take into account variation in donor-recipient relationship, as different relationships may influence the type and amount of benefits that a donor might receive from LKD. We posit that donors who share a household with and have direct care responsibilities for an ESRD patient may accrue a wider range of, and more tangible benefits than someone with less direct contact or fewer responsibilities. To capture this sense of connectedness and responsibility that some potential donors have for their recipients, we propose donors in shared households with caregiving responsibilities be termed "interdependent donors." That is, their wellbeing and that of their potential recipient are connected to and interdependent on each other.

Our contention is that tangible benefits experienced by interdependent donors are not limited to the emotional benefits that have been the focus of prior research (9–11). Interdependent donors may experience more tangible benefits or measurable improvements in quality of life as a result of reductions in stress, strain and caregiving burden, and spousal donors may also experience improvements in marital quality and social life. Furthermore, both the donor's and recipient's ability to work and therefore their productivity and financial situation may both be improved (2). While prior studies have demonstrated that donors expect and experience benefits in personal growth, interpersonal relationships, mental health and spiritual life (9–11), we believe that study of donor experiences beyond the psychosocial may reveal previously neglected benefits.

Interdependent donors may encompass a large variety of relationships, but spouses and partners provide a compelling example of how one person's wellbeing can depend on another's. A model for donor evaluation and selection that takes into account tangible benefits realized by interdependent donors in tandem with an empirical risk assessment would more fully encompass the impact of the LKD experience for both recipients and donors. This model would more accurately reflect the real lives of donors and recipients and the prospects for benefits realized through donation, and is therefore a more appropriate approach to LKD evaluation and selection.

In semi-structured interviews conducted as part of our ongoing study of spouses and partners of transplant candidates and recipients, a wife who donated to her husband explained that her motivation for donating was the "change in our lifestyle… You're chained, you're held hostage by that dialysis machine! And we both work full time, we're active, and your whole life revolved around that machine." Indeed, past research has shown that spouses and partners of ESRD patients are at an increased risk of caregiving burden, marital strain and decreased mental health (12–14). Another spouse explained her change in mood before her husband's transplant, saying "…you grieve, you're grieving for someone that's still alive, it's hard to go through the motions… you're dying inside but you're still alive." And now, nine months after her husband's transplant, the participant said she is "Joyful! … Nobody can steal my joy!"

As one caregiver described it, a spouse starting dialysis can lead to “a seismic change.” For interdependent donors, one major benefit of transplantation may be a return to normalcy after a long period of time spent caring for a partner on dialysis. Due to shared interests and needs in interdependent relationships, the recipient’s outcomes will have a direct impact on the donor’s quality of life (15). The KT recipient’s return to work, for example, may be a measurable proxy for this return to normalcy; past research has shown that employment rates are higher after transplantation than before (10), that the majority of KT recipients are fit for the job they performed before transplant, and that most are fit to do so without any special accommodations (11). A model of risk-benefit balance in LKD must acknowledge that tangible benefits for interdependent donors are realized by individuals and by the entire household.

CALL FOR RESEARCH: TOWARD A FULLER RISK-BENEFIT ASSESSMENT

There is a lack of empirical assessment of the benefits that accrue from KT to donors and caregivers in interdependent relationships. Consistent with assumptions underlying a framework that focuses on acceptable risk, prior prospective and retrospective studies on donor outcomes have been primarily concerned with minimizing risk. Indeed, thorough donor follow-up is crucial to the implementation of our proposed framework. Research on other procedures suggests that caregivers do realize quality of life (QOL) benefits from medical and surgical procedures undergone by patients for whom they are responsible (16–20). This suggests that beyond direct medical benefits to the patient, some tangible benefits flow to caregivers. Studies addressing benefits of LKD for the donor are limited to assessing psychosocial outcomes such as improved self-esteem, relationships and mental health (9–11), and do not address other direct effects, such as changes in caregiving burden and home environment.

Various studies have shown that caregivers of dialysis patients can experience changes in social interactions (21, 22), finances (21, 22), careers (21), eating habits (21), sexual activity (21), family tensions (22), responsibilities of children (22), mental health (23–25) and sleep patterns (24, 25) following the onset of dialysis. ESRD and dialysis affect nearly every aspect of both the patient and caregiver’s life. Spousal caregivers in particular experience significant burdens of disease and caregiving responsibilities. Chronic disease in one partner is observed to create strain within married couples (12, 26, 27) which has subsequent implications for the quality of care provided by spousal caregivers (14). When asked if he had learned any life lessons from caring for his wife, the husband of a dialysis patient responded “Yes, and it’s a harsh one. But I was warned before, by my partner, don’t get involved with anyone that’s ill.” Cross sectional and retrospective studies observe caregivers of transplant patients to have lower caregiving burden and improved quality of life (QOL) compared to caregivers of dialysis patients (14, 24, 25). These observed measurable changes in caregivers’ QOL suggest that KT, while improving the patient’s independence and freeing them from the burden of dialysis, could also significantly improve caregiver QOL. Prospective research on QOL benefits of KT to caregivers in general, and interdependent donors in particular is needed.

CONCLUSION

The implementation of a donor evaluation and selection framework that seeks to balance the full scope of the risks and benefits of LKD would have important implications for clinical practice. We envision that a risk-benefit assessment scale that takes into account the tangible benefits that may accrue to interdependent donors, developed using rigorously collected qualitative and quantitative data, will better inform transplant center-level decisions during the donor evaluation and selection process. As noted above, the data required to inform such a scale needs to be collected. We do not propose the empirical exploration of donor benefit in an effort to artificially skew the assessment of acceptable risk-benefit balance in LKD. Rather we hope to provide a more accurate assessment of donor risks and benefits to inform LKD evaluation and selection. An “interdependent” relationship, as we have described, may manifest in a variety of ways. Further refinement of what constitutes interdependency may be required to aid clinical decision-making, and any such definition should be informed by the empirical research described above.

Within the United States, there is variation in how transplant centers approach acceptable risk to donors. Furthermore, individual practitioners are prone to personal and emotional biases that may affect LKD evaluation and the acceptability of individual donors. Our proposed framework may reduce some of this variability by providing a shared structure for the evaluation of many factors that are currently difficult to assess empirically. As motivations for donation are culturally specific and vary globally, our proposed approach is intended for practice in the United States. However, other countries may also benefit from a framework of risk-benefit balancing that considers the risks and benefits as experienced by their populations.

While others have previously argued for balancing minimization of risk and respect for autonomy in LKD, recent discussions highlight the need to more fully consider potential donor benefits. We advance this approach, and posit that interdependent donors may experience tangible benefits after donation that could justify allowing greater levels of risk than would be allowable by assessments that focus on minimization of risk and autonomous decision making alone. This proposed framework will allow both normative and empirical inquiry to inform and to more fully promote donor decision making within a framework for LKD assessment where both risks and benefits are appropriately considered as part of LKD evaluation and selection.

ABBREVIATIONS

ESRD	end-stage renal disease
KDIGO	Kidney Disease Improving Global Outcomes
KT	kidney transplant
LKD	live kidney donation
OPTN	Organ Procurement and Transplantation Network

UNOS	United Network for Organ Sharing

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