

SOUNDING BOARD

Informing Candidates for Solid-Organ Transplantation about Donor Risk Factors

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For the first time in 15 years, there has been documented transmission of the human immunodeficiency virus (HIV) through solid-organ transplantation.¹ Although transmission of infectious agents through transplantation is rare,² such cases raise important questions about how informed consent for transplantation should be obtained and about the type of resource that transplantable organs represent.

Among the questions raised are the following: Should potential recipients be informed about the general risks associated with transplantation or those specifically associated with an identified organ? Should the risks engendered by the behavior of donors be treated differently from those associated with the medical profiles of donors? Finally, is the supply of transplantable organs a singular public good to be distributed to maximize public health or is it a market of intermittently available goods from which eligible recipients might select in order to maximize their own well-being?

THE CHICAGO CASE

A 38-year-old man died after a motor vehicle accident in January 2007. His liver, heart, and both kidneys were subsequently transplanted into four recipients. At the time of the donor's death, all routine tests for transmittable diseases² were negative. However, the local organ-procurement organization and the transplantation surgeons to whom the organs were sent knew that this donor had a behavioral risk factor that increased the possibility that the antibody-based assays for HIV and other viruses might show false negative results.^{1,3}

All four organ recipients have since tested positive for both HIV and the hepatitis C virus (HCV). At least one of the recipients is considering a suit against the transplantation center and the local organ-procurement organization, charging that

she was harmed by not being notified of the donor's above-average risk of HIV and, therefore, was denied the opportunity to decline the donation. Her attorney has declared, "it's up to the patient . . . to make the decision whether to incur the risk."³

BEHAVIORAL RISKS AMONG DONORS

A well-known limitation of the safety of organ transplantation is that antibody-based tests to detect viruses have poor sensitivity within the first few weeks after infection.² Although more sensitive nucleic acid–amplification tests are now used in some regions, even these tests do not fully eliminate the possibility of a false negative result. Data from studies involving tissue donors show that between 1 of 55,000⁴ and 1 of 161,000⁵ donors are infected with HIV, despite negative antibody-based tests, and that the addition of nucleic acid testing reduces the rate of false negative results by two thirds.^{4,5}

Certain donors have above-average risks of false negative HIV tests because their behaviors may generate more new infections. Nonetheless, persons with risk factors for HIV that have been identified by the Centers for Disease Control and Prevention (CDC)⁶ are commonly donors for solid-organ transplantation. Table 1 indicates that during the period from 1995 to 2006, 6% of donors in our donor service area had risk factors that were consistent with the CDC criteria.

BEHAVIORAL VERSUS MEDICAL DONOR RISKS

Donors with behavioral risk factors are not barred from contributing to the organ supply, as they are from contributing to the blood supply,⁷ because scarcity is a much more salient feature of the or-

Table 1. Deceased Donors Who Have Nonstandard Criteria and Outcomes of Patients on the Waiting List, 1995–2006.*

Year	Donors with Nonstandard Criteria				Deaths or Removals of Patients from Waiting List (N = 4619)
	CDC High-Risk (N = 236) [†]	Expanded-Criteria (N = 1048) [‡]	DCDD (N = 390) [§]	CDC High-Risk, Expanded-Criteria, or DCDD (N = 1635) [¶]	
	<i>no. of donors/total no. (%)</i>				<i>no.</i>
1995	9/222 (4)	54/222 (24)	2/222 (1)	64/222 (29)	212
1996	10/261 (4)	67/261 (26)	12/261 (5)	85/261 (33)	263
1997	11/291 (4)	66/291 (23)	14/291 (5)	90/291 (31)	311
1998	22/295 (7)	73/295 (25)	25/295 (8)	117/295 (40)	332
1999	21/329 (6)	96/329 (29)	24/329 (7)	138/329 (42)	373
2000	20/298 (7)	89/298 (30)	23/298 (8)	128/298 (43)	463
2001	20/314 (6)	77/314 (25)	32/314 (10)	125/314 (40)	450
2002	27/354 (8)	107/354 (30)	36/354 (10)	165/354 (47)	468
2003	22/344 (6)	100/344 (29)	51/344 (15)	171/344 (50)	421
2004	26/387 (7)	110/387 (28)	47/387 (12)	178/387 (46)	455
2005	20/382 (5)	97/382 (25)	57/382 (15)	171/382 (45)	437
2006	28/401 (7)	112/401 (28)	67/401 (17)	203/401 (51)	434

* Data are from the Gift of Life Donor Program. A total of 10,863 organs were transplanted from 3878 donors during the 12-year period. CDC denotes Centers for Disease Control and Prevention, and DCDD donation after circulatory determination of death.

[†] High-risk donors are any donors meeting one of the following seven criteria of the CDC⁶: men who have had sex with another man in the preceding 5 years; persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 years; persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates; persons who have engaged in sex in exchange for money or drugs in the preceding 5 years; persons who have had sex in the preceding 12 months with any person described in the first four criteria or with a person with suspected HIV infection; persons who have been exposed in the preceding 12 months to known or suspected HIV-infected blood through percutaneous inoculation or through contact with an open wound, nonintact skin, or a mucous membrane; and inmates in correctional systems (i.e., jail or a correctional facility) for at least 72 hours in the preceding 12 months.

[‡] An expanded-criteria donor fulfills expanded criteria according to the United Network for Organ Sharing policy for kidney donation and is not a DCDD donor.

[§] A total of 44 of 390 DCDD donors (11%) also fulfilled expanded criteria.

[¶] The number of patients in this category is lower than the sum of the numbers of CDC high-risk and DCDD donors because these criteria are not mutually exclusive; 3% of all patients with expanded and DCDD criteria also met the risk criteria of the CDC.

^{||} Patients who died while on the waiting list or were removed from the waiting list because they became too sick to undergo transplantation are included; patients removed for other reasons are excluded.

gan supply. Indeed, approximately 10% of all patients on the waiting list for solid-organ transplantation die each year without receiving an organ.⁸

The inclusion of donors with behavioral risk factors is merely one of many policies intended to narrow the growing gap between the supply of and demand for transplantable organs. For example, donation after circulatory determination of death (DCDD) is a common source of organs for transplantation (Table 1). In these cases, organ perfusion ceases before organ procurement, yielding short periods of warm ischemia. Recipient and

graft survival after DCDD appear to be similar to the outcomes associated with more traditional donation from brain-dead donors for kidneys⁹⁻¹² and pancreases,¹² but these outcomes are slightly worse for DCDD livers.¹³⁻¹⁵ As experience grows with transplanting hearts¹⁶ and lungs^{17,18} after DCDD, differences in the outcomes associated with these organs may emerge.

Donors with “expanded criteria” are also increasingly contributing to the organ supply (Table 1). These donors have one or more clinical risk factors such as advanced age, obesity, or hyperten-

sion; these risk factors may portend worse outcomes of transplantation. The degrees to which these risk factors reduce graft and recipient survival have been defined for kidney¹⁹ and liver²⁰ transplantation, and definitions of expanded-criteria donors are being established for the transplantation of other organs.²¹⁻²³

If unblemished, or “standard-criteria” donors were plentiful, there would be no need to use riskier organs from DCDD, donors with expanded criteria, or donors with behavioral risk factors. However, the rate of death among patients on the waiting list remains high despite the fact that the organ supply has approximately doubled in recent years through the use of organs from donors with nonstandard criteria (Table 1). The modest costs to individual recipients associated with the use of organs from DCDD and expanded-criteria donors have been widely accepted²⁴⁻²⁸ because each additional deceased donor contributes approximately 30 life-years to society.²⁹

Although the consequences of using organs from donors with behavioral risk factors are uncertain, in the era of highly active antiretroviral therapy, these risks are probably smaller than those associated with using organs from expanded-criteria donors. Indeed, the survival of HIV-infected patients who have received transplants is similar to that of recipients who are not infected.³⁰⁻³² Nonetheless, because the risks of transmitting HIV and other infections are unlikely to be eliminated,² we think the question is not whether potential recipients should be informed of these risks, but when.

MODELS OF DISCLOSURE OF RISKS

Disclosing the risks and benefits of solid-organ transplantation and obtaining informed consent from patients might occur when the patient is placed on the waiting list, when an organ is offered, or at both times. To a limited extent, consent obtained at the time of listing is already required by a United Network for Organ Sharing (UNOS) policy stating that prospective kidney recipients must designate before listing whether they would accept organs from expanded-criteria donors.³³ However, there is substantial regional variation in this practice, with between 2% and 95% of candidates listed as accepting organs from expanded-criteria donors across the 58 donor service areas.³⁴ The risk-disclosure practices of transplan-

tation programs are unknown and unregulated with regard to all other organs. Within our own donor service area, the formality and timing of consent processes vary widely among programs.

Because variability among consent practices when patients are placed on the waiting list influences the odds that candidates will receive non-standard organs,³³ standardization is needed to ensure the system's equity. Standardization would also promote the autonomy of recipients by helping to ensure that they are informed of all relevant donor risk factors. The promotion of autonomy also underlies the argument that consent should be obtained when a specific organ is offered so that the patient may weigh its unique characteristics and then accept or reject it accordingly. UNOS currently requires such organ-specific disclosure when an organ is offered from a donor who is at high risk for HIV infection according to the CDC's criteria.³⁵ With enthusiasm growing for the organ-specific disclosure of risk,³³ similar policies might soon be developed for the disclosure of other organ characteristics, either in lieu of or in addition to consent at the time of listing.

However, at least three important problems are associated with relaying organ-specific risks to patients. First, the disclosure of organ-specific risks may not increase the ability of patients to make welfare-promoting decisions. Not only would patients have little time to consider the risks and benefits of accepting or declining a particular organ before it was offered elsewhere, but the estimates of risks themselves would be highly uncertain. Although multivariable indexes of risk are available to help determine the prospects for long-term graft and patient survival among recipients of livers and kidneys from expanded-criteria donors,^{19,20} predictive models are notoriously imprecise when they are applied to individual patients.³⁶

Reported donor risk factors for HIV and other infections are even less certain. By labeling as “high-risk” all donors with one of several different behaviors (Table 1), the current system does little to help patients quantify this risk. Furthermore, the veracity of reported behavioral risk factors is limited because this information is typically obtained from grieving family members who may not know of or acknowledge their loved one's behaviors. Indeed, the last known case of HIV transmission through organ transplantation was from a donor with no identified risks for HIV.³⁷ Thus,

allowing patients to decline organs from patients with reported risk factors would not fully protect them against HIV transmission.

The second problem with the organ-specific disclosure of risk is that some patients might select organs not on the basis of actual risk, but on the basis of more nebulous aversions to stigmatized donors such as homosexual men. Thus, permitting patients to evaluate specific donor characteristics could wrongly establish social bias as a legitimate rationale for guiding the allocation of a public good.

Finally, because the organ-specific disclosure of risk requires extra time precisely when time is at a premium, it could prevent the optimal use of the organ supply. Any delays from the time a donor is identified to the time of transplantation may prolong graft ischemia and reduce opportunities for finding an optimal recipient with the use of criteria such as blood type, HLA matching for kidneys, or body height for lungs. Even modest delays resulting from organ-specific consent would be difficult to justify in view of the strong moral bases^{30,38,39} and broad public support⁴⁰ for maximizing efficiency in the allocation of scarce organs.

THE RIGHT TO PROSPECTIVELY DECLINE NONSTANDARD ORGANS

The national adoption of a comprehensive model for the disclosure of risks and consent would promote the efficient and equitable allocation of organs while respecting the individual values and preferences of patients. We propose that UNOS rapidly implement a policy requiring that transplantation programs disclose all foreseeable risks of transplantation to potential recipients when they are placed on the waiting list and that patients be allowed to choose to accept or decline organs from any nonstandard-criteria donor.

Allowing patients to make a prospective choice to accept or decline nonstandard organs respects patients' preferences without creating the inefficiency, inequity, and potential for abuse that would ensue if patients were allowed to select individual organs when they were offered. A dichotomous choice, whereby all nonstandard organs are considered as a group, has several additional advantages. First, it is flexible to changes in the definitions of "standard" organs over time. Second, it

avoids the creation of an erroneous perception of certainty regarding the contribution of each risk factor to the absolute or relative risks associated with a particular organ. Third, by combining the behavioral and medical risks of donors, this approach minimizes the influence of social biases on organ acceptance.

An exception to this rule would be needed for recipients for whom a specific type of nonstandard organ confers no increased risk. For example, receiving a kidney from an HCV-infected donor does not alter the outcome for an HCV-infected recipient,⁴¹ so such recipients should be allowed to accept organs from donors with behavioral risks while declining organs from expanded-criteria and DCDD donors.

In all cases, physicians would need to ensure that patients understand that declining nonstandard organs may delay their receipt of an organ, possibly even resulting in death before a standard-criteria organ becomes available. In our donor service area, patients would need to understand that forgoing organs from donors with medical and behavioral risks would approximately halve the supply of organs available to them (Table 1). Because such estimates will vary according to organ and geographic region, each transplantation program should provide its own relevant estimates to patients.

Finally, patients who decline organs from donors with nonstandard criteria should also indicate whether they would accept such organs if their clinical condition changed. Despite this safeguard, transplantation physicians may ultimately have to use personal judgment to determine the risks and benefits of providing a particular organ to a particular patient. In unique circumstances, there is no substitute for deferring to clinical judgment guided by the fiduciary responsibilities of physicians to their patients.⁴²

Transplantation physicians might be tempted to "game" the system when given latitude in decisions regarding placement of patients on the waiting list.⁴³ For example, they might encourage their patients to accept organs from donors with nonstandard criteria while promising that they themselves would reject all but the least risky organs. However, external review should be able to identify any aberrations, and implementing more specific listing policies might prevent further problems.⁴³

Table 2. Aspects of Solid-Organ Transplantation That Should Be Disclosed during the Consent Process.

Known risks of transplantation include the rare risks of transmission of HIV, hepatitis B virus, hepatitis C virus, and other infectious agents.
Because of the scarcity of organs, organs from expanded-criteria donors, donors after circulatory determination of death, and donors with a slight risk of certain infections are sometimes used.
Patients may decline nonstandard-criteria organs, but doing so may delay their receipt of an organ and possibly even result in death while they are on the waiting list.
Physicians' understanding of donor characteristics that confer risk is incomplete and continually evolving.
New risks may arise in the future (e.g., as new transmittable infections are identified), and all efforts to minimize these risks will be made.

ENSURING EQUITY

Our proposal, like the organ-specific model of disclosure of risk, might be limited in equity if it caused organs from donors with behavioral or medical risks to be diverted to patients who are more accepting of risk. Consider a donor service area in which five patients are listed as having highest priority (i.e., UNOS status 1A) for heart transplantation. One of these patients has declined nonstandard organs and four have accepted such organs. If a nonstandard organ were offered first to the patient who declined nonstandard organs, it would be diverted to one of the members of the group who was more accepting of risk, whereas a standard organ would be retained. Although enabling the first patient to act on his own level of risk aversion would promote his autonomy, this policy would be unjust if his decision caused adverse consequences for patients who were more accepting of risk.

Research is therefore needed to ensure that patients who accept nonstandard organs do not have worse risk-adjusted outcomes as compared with those who accept only standard organs. We might expect patients who accept risk to fare better than those who do not because they would have a greater chance of receiving organs.³⁴ However, in the unlikely event that patients who accepted all organs had worse long-term outcomes, UNOS would have to consider restricting the ability of patients to opt out of receiving nonstandard organs in order to maintain equity in the allocation of this shared public good.⁴⁴

CONCLUSIONS

Standards for the disclosure of risk and consent in solid-organ transplantation require far more standardization and formality than are currently available. UNOS should develop a single policy that requires a comprehensive consent process when all candidates for transplantation are placed on the waiting list. This policy should outline specific aspects of transplantation that should be disclosed during the consent process (Table 2), allow patients to make a dichotomous choice to accept or decline all nonstandard organs as a group, and eliminate the practice of organ-specific consent. In particular, we believe UNOS should abandon its current recommendation that patients be notified when organs are offered from donors with behavioral risk factors. Finally, evidence of compliance with this policy should be required for transplantation programs to retain UNOS membership.

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