HHS Public Access

Author manuscript

Am J Kidney Dis. Author manuscript; available in PMC 2016 July 01.

Published in final edited form as:

Am J Kidney Dis. 2015 July ; 66(1): 23–27. doi:10.1053/j.ajkd.2015.01.032.

Living Kidney Donors and ESRD

Lainie Friedman Ross, MD, PhD

Departments of Pediatrics, Medicine, Surgery and the MacLean Center for Clinical Medical Ethics, University of Chicago

Abstract

There are over 325 living kidney donors who have developed end-stage renal disease (ESRD) and have been listed on the Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS) deceased donor kidney wait list. The OPTN/UNOS database records where these kidney donors are listed and, if they donated after April 1994, where that donation occurred. These two locations are often not the same. In this commentary, I examine whether a national living donor registry should be created and whether transplant centers should be notified when one of their living kidney donors develops ESRD. I consider and refute 5 potential objections to center notification. I explain that transplant centers should look back at these cases and input data into a registry to attempt to identify patterns that could improve donor evaluation protocols. Creating a registry and mining the information it contains is, in my view, our moral and professional responsibility to future patients and the transplant endeavor. As individuals and as a community, we need to acknowledge the many unknown risks of living kidney donation and take responsibility for identifying these risks. We then must share information about these risks, educate prospective donors about them, and attempt to minimize them.

Keywords

living donors; donor registry; end-stage renal disease (ESRD); kidney; transplantation; duty to look back; donor risks; Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS)

Early Recordkeeping on Living Kidney Donation

The first successful living kidney donation was performed by Murray and colleagues on December 23, 1954 between identical twin brothers, Ronald and Richard Herrick.[1] Murray and colleagues coordinated a voluntary registry as an adjunct to the Human Kidney Transplant Conference sponsored by the National Academy of Sciences-National Research Council in September 1963. In the fourth registry update, published in 1965, data were

Corresponding author: Lainie Friedman Ross, MD, PhD, University of Chicago, 5841 S Maryland Ave, MC 6082, Chicago IL 60637, Lross@uchicago.edu.

Financial Disclosure: The author declares that she has no relevant financial interests.

tabulated regarding 672 primary transplants, 45 secondary transplants and 2 tertiary transplants, for a total of 719 transplants in 672 patients.[2] The registry was transferred over to the American College of Surgeons in 1970 with funding from the National Institutes of Health.[3] At the time, the registry had data on more than 3,600 transplants. The only data about the living donors provided in any of the reports focused on perioperative outcome data.[3] The registry reports stopped in June 1976 with the 13th iteration, which included voluntary data from 301 institutions, 165 of which were in the United States.[4] At the time, registry data existed for over 25,000 kidney transplants with deceased donors as the major source of organs.[4]

In 1971, Dr. Paul Terasaki at University of California at Los Angeles (UCLA) started another data registry. The UCLA International Transplant Registry included data of kidney transplants submitted voluntarily from more than 130 centers in the United States, Canada, Europe and Japan.[5] This registry continued through the early 1990s, but did not include any outcome data on living donors.[6]

In the United States, the National Organ Transplant Act (NOTA) was passed in 1984 and created a national system for organ procurement and allocation.[7] Through NOTA, Congress delegated the execution of policy to the Organ Procurement and Transplantation Network (OPTN), which has, since its establishment, been run by the United Network for Organ Sharing (UNOS). However, it was not until 1994 that the OPTN began collecting social security numbers of living donors; individuals who donated prior to this are “impossible to track.”[8] Beginning in 2000, the OPTN required transplant centers to collect one year of follow-up data on living donors, which was expanded to 2 years in 2006.

ESRD After Living Kidney Donation

Challenges in Estimating Risk

Despite the lack of systematic long-term data collection on living donors, 2 recent publications have examined the long-term risks of living kidney donation.[9,10] While there are disagreements about the appropriate control group for such studies and whether risk should be discussed in absolute or relative terms, one fact is not disputed: long-term outcome data on the first 6 decades of living kidney donation in the US are incomplete, and data collection for only 2 years is insufficient for understanding longer term risks.

In 2011, the UNOS database documented 325 individuals who had been living donors, had developed end stage renal disease (ESRD), and were listed for a deceased donor kidney transplant (for which they were given four additional wait list points). The significance of the number 325 is complicated by the fact that neither the actual denominator (how many individuals have served as living donors) nor the actual numerator (how many living donors have developed ESRD) is known. The denominator is not known because until 1994, data on living donors was not routinely collected (however, given the data that exist, a reasonable estimate would be that 150,000 living donor transplants have occurred over the past 60 years in the United States). The numerator is not known because the UNOS database only includes living donors who experienced kidney failure after 1996, when the policy of giving waitlisted living donors 4 additional points went into effect. The UNOS database does not

include living donors who developed ESRD before 1996, donors who developed ESRD but chose not to get wait listed for a deceased donor kidney, or those who died before getting on the wait list. However, even if the actual number of living kidney donors with ESRD is twice (650) or ten-fold (3,250) the number identified by UNOS, these values are still quite low given the large number (albeit an approximation) of living kidney donors.

In a publication from 2014, Muzaale et al compared the lifetime risk of ESRD in donors, healthy non-donors, and the general population. [10] Using data from April 1994 to November 2011, the authors calculated the risk of developing ESRD in living donors by linking the UNOS database to Centers for Medicare & Medicaid Services data, then compared with NHANES (National Health and Nutrition Examination Survey) data, Living donors had a 0.9% lifetime risk of developing ESRD, which is lower than the risk in the general population (3.26%) but 8-fold higher than that in healthy non-donors (0.14%). However, these data are limited, as donors were followed up for a median of only 7.6 years.

Why Transplant Centers May Be Unaware of Donors Who Have Developed ESRD

After a thorough vetting by the Health Resources and Services Administration (HRSA), my colleagues and I obtained protected health information (PHI) about the 325 waitlisted living donors identified by the UNOS database. For each individual, we were provided with name, date of birth, and location of listing for a deceased donor transplant. We are now locating these individuals and, for those who consent for our study, we are collecting health records and blood samples to determine if there are biomarkers or genetic factors that may explain why some living donors develop ESRD.

In talking to dozens of these individuals, we realized that often the donor wasn't listed as a transplant candidate at same center where donation occurred. There are a variety of reasons that this may be the case. The donor may have moved post donation; donated at a hospital much closer to the recipient than the donor; or have insurance that only covers care from a particular hospital. Alternatively, the donor's original transplant program may have dissolved; a primary care physician or nephrologist may have referred the donor to a specific program; or the patient simply may not have wanted to return to the center where donation occurred.

Many of these living donors have not disclosed their kidney disease to the center at which they donated. This is not surprising, since they often are no longer receiving health care at the original facility, especially if years or decades have passed since the donation. But the lack of follow-up data complicates the transplant community's ability to fully understand the risks of living kidney donation. A review of these cases in light of the donors' subsequent kidney failure can only take place if programs are aware of such a development.

This is not about blaming the centers for inadequate work-ups or for having too liberal a donor acceptance policy. All donors undergo a medical and psychological work-up, which has become more rigorous over time. Currently, at a minimum, all potential living donors have to pass screening by a nephrologist, transplant surgeon, living donor advocate, and transplant social worker. Any concerns raised by this screening must be resolved before the candidate is approved to serve as a living donor. Most of the donors with whom I have

spoken would donate again, even knowing their destiny. Rather than assigning blame, the reason to make programs aware is to enable them to review the records of donors who developed kidney failure to determine if there were factors that should have led to caution (or if the donor's risks were truly unpredictable).[11]

Should Transplant Centers Be Informed of Donors Who Have Developed ESRD?

Given that HRSA has entrusted me and my colleagues with the PHI of these donors, I could contact transplant programs with this information and ask them to review these records. The rationale for this is based on our moral obligations to living donors, past and present. Ethically, the transplant community needs to look back to understand, if possible, why some donors develop ESRD; to determine whether the kidney donation itself may have catalyzed or accelerated kidney disease in these individuals; and, most importantly, to learn if we can minimize this event in the future. I believe that this can only happen if the transplant programs know that this has happened to one of their own and join together to identify possible red flags or recurrent patterns.

When I have proposed contacting transplant programs regarding living donors who have developed ESRD, colleagues object on five distinct grounds. First, they point out that the donation may have occurred decades before ESRD development, so that the transplant teams, screening tools and protocols, and clinical understanding have entirely changed, reducing the clinical benefit of retrospective study. I would argue that despite these changes, medical records, consultations, and laboratory results are still worth reviewing for potential insights.

Second, colleagues object that each center will have only a few patients that progress to ESRD such that no single center will be able to collect enough data to find any patterns. They are most likely correct. But while this may not be instructive for the current transplant professionals at the site (that is, those who were not involved in the decision to proceed with the particular donor), it may be the only way for the transplant community to collect data from a large percentage of cases in which donors developed ESRD, and points to the need for a longitudinal national database to which all can contribute.[12]

Third, colleagues contend that donors who change transplant programs are no longer patients of the original program, so it would be a violation of privacy laws (Health Information Portability and Accountability Act [HIPAA]) to contact the initial center. They are misguided. For the vast majority of donors who have enrolled in our study, I have permission from HRSA, the University of Chicago Institutional Review Board, and the donors themselves to contact their previous health care providers for information. Such requests are usually directed to a medical records office, which typically sends the information without reviewing it. Since my proposal involves contacting the transplant programs as well so that they can try to identify factors that might explain why donors have developed ESRD, one might argue that such review constitutes a privacy violation. This is not the case. The transplant team has the right (and I would add, the responsibility) to look back at charts for quality improvement. Quality improvement studies performed by reviewing medical records do not need informed consent of patients. Moreover, I believe that the transplant team should make a good-faith effort to ensure that the data provided by

their institution accurately reflect donor evaluation and assessment. For instance, some teams may also have shadow records[13]; common in the past, these files were separate from the hospital chart and may contain additional transplant-focused information (social, psychological, or environmental in nature) that the team or patient did not want documented in the clinic chart, which can be accessed by many others in the health care system.[14] These shadow charts may have information important for understanding the donor selection process that may not otherwise be available.

Fourth, some colleagues object that even if my proposal does not violate privacy laws, transplant centers have no legal obligation to look back. While that may be true, centers may have a moral obligation to re-analyze their decision to accept as a living donor a patient who subsequently developed kidney failure. By undertaking this review, the centers could determine if there are patterns that might be useful in future evaluations and that might help to minimize risks to future donors.

Fifth, some colleagues may object that if centers reanalyze the PHI of former patients, they would be obligated to report results to the donors. Expert guidelines regarding the return of results have been developed by the genetics community.[15,16] The consensus is that not all secondary findings (those unexpectedly discovered when performing a physical exam or medical test for a different purpose) should be returned to patients; instead, only “actionable information” (that which is thought to be immediately relevant to the future health of the individual) should be relayed. [16,17] In the scenario being considered, the possible identification of modifiable ESRD risk factors is not actionable information because the donor has already developed ESRD. However, re-examination might reveal secondary findings for which it may not be clear whether the information was shared with the donor at the time of the work-up (e.g., hemoglobin electrophoresis to screen the potential donor for the sickle cell trait might show the donor to be a carrier of hemoglobin C).[18] Alternatively, there might be secondary findings of unrecognized significance at the time of data collection and evaluation (e.g., low bone density determined by radiographic review). Do these findings need to be reported to the donor? Ideally, donors would be asked during their work-up whether they would want such information. Given that the transplant community has never had policies regarding reexamination of PHI and re-contact of donors, it is reasonable not to return secondary findings at this time. Moving forward, however, transplant physicians will need to consider discussing and documenting the attitudes of prospective living donors about the possibility of re-contact such that preferences are known and respected even with changes in health care providers.

The Case for a National Living Kidney Donor Registry

As detailed in the preceding, my position is that the transplant community has a moral duty to look back from a continuous quality improvement perspective to try to understand why some donors develop ESRD. We may learn that for some donors, this adverse outcome was just “bad luck”. Alternatively, we may learn that certain genetic variants or some combination of clinical laboratory values (e.g., low normal glomerular filtration rate and high normal blood pressure or familial diagnoses) place individuals at greater risk for ESRD post–unilateral nephrectomy. The numbers at any center will be too small to identify

recurrent patterns hitherto unappreciated. In fact, even if the data are aggregated into a registry, the numbers may be too small to produce statistically significant results. Nevertheless, the registry data, which will only grow with time, may suggest endpoints for future prospective studies. We may learn about some new risk factors that would modify our current donor evaluations. Given the widening gap between supply and demand, many programs are now accepting less-healthy donors than was permitted in previous years, making long-term follow-up even more important.[19,20] Only by collecting all of the individual data and developing a national registry that contains longitudinal data about all living donors will we be able to fully understand the long-term risks of unilateral nephrectomy. UNOS, which already collects two-year follow up data, may be the right organization to coordinate the registry. However, transplant centers will need to be motivated to collect and send the data to the registry, regardless of who maintains it.

In sum, our moral and professional responsibility to future patients and to the transplant endeavor compels us to try to discover why certain living kidney donors go on to develop ESRD. Going forward, transplant physicians need to inform living kidney donors that their donation may pose increased but unknown risks to long-term health and that the work-up cannot identify risks that are currently not appreciated. As a community, transplant professionals need to take responsibility for identifying the risks of living kidney donation, to share and educate prospective donors about these risks, and to attempt to minimize them.

Acknowledgments

I would like to thank Walter Glannon, PhD and J. Richard Thistlethwaite, Jr, MD, PhD for comments on earlier drafts, and the anonymous reviewers of *AJKD* for their helpful critiques.

Support: Research reported in this publication was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health (NIH) under Award Number UL1TR000430. The content herein is solely the responsibility of the author and does not necessarily represent the official views of the NIH. This article was also supported by a Robert Wood Johnson Investigator Award in Health Policy, “A Case-Based Approach to the Ethical and Policy Issues Raised by Living Donor Transplantation”.

References

1. Murray JE, Merrill JP, Harrison JH. Kidney Transplantation Between Seven Pairs of Identical Twins. Ann Surg. 1958; 148(3):343–59. [PubMed: 13571912]
2. Murray JE, Gleason R, Bartholomay A. Transplantation Proceedings: Fourth Report of Human Kidney Transplant Registry, 16 September 1964 to 15 March 1965. Transplantation. 1965; 3(5): 684–699.
3. Murray JE, Barnes BA, Atkinson JC. Eighth Report of the Human Kidney Transplant Registry. Transplantation. 1971; 11(3):328–337. [PubMed: 4934267]
4. Advisory Committee to the Renal Transplant Registry. The 13th report of the human renal transplant registry. Transplant Proc. 1977; IX(1):9–26.
5. Kaneku H, Terasaki PI. Chapter 1: A Review of the Past 25 Years of “Clinical Transplants”. Clin Transpl. 2009:1–39. [PubMed: 20527067]
6. Cecka JM. Chapter 30: Living Donor Transplants. Clin Transpl. 1995:363–377. [PubMed: 8794280]
7. National Organ Transplant Act (NOTA), Public Law 98-507, Oct. 19, 1984, 98 Stat. 2339.
8. [Accessed January 19, 2015] Living Donor 101. On the web at: http://www.livingdonor101.com/kidney-failure-risk.shtml
9. Mjøen G, Hallan S, Hartmann A, et al. Long-term risks for kidney donors. Kidney International. 2014; 86:162–167.10.1038/ki.2013.460 [PubMed: 24284516]

10. Muzaale AD, Massie AB, Wang MC, et al. Risk of end-stage renal disease following live kidney donation. JAMA. 2014; 311(6):579–86. [PubMed: 24519297]
11. Steiner RW, Ix JH, Rifkin DE, Gert B. Estimating risks of de novo kidney diseases after living kidney donation. Am J Transplant. 2014; 14(3):538–44. [PubMed: 24612746]
12. Ross LF, Siegler M, Thistlethwaite JR Jr. We need a registry of living kidney donors. Hastings Center Report. 2007; 7(6):1. p following 48. On the web at: http://www.bioethicsforum.org/living-kidney-donation-long-term-risks-registry.asp. [PubMed: 18179104]
13. Balka E. Ghost charts and shadow records: implications for system design. Stud Health Technol Inform. 2010; 160(Pt 1):686–90. [PubMed: 20841774]
14. Siegler M. Confidentiality in medicine: A decrepit concept. N Engl J Med. 1982; 307(24):1518–1521. [PubMed: 7144818]
15. Bookman EB, Langehome AA, Eckfeldt JH, et al. Reporting Genetic Results in Research Studies: Summary and Recommendations of an NHLBI Working Group. Am J Med Genet. 2006; 140A: 1033–1040. [PubMed: 16575896]
16. Fabsitz RR, McGuire A, Sharp RR, Puggal M, Beskow LM, Biesecker LG, et al. for the National Heart, Lung, and Blood Institute working group. Ethical and practical guidelines for reporting genetic research results to study participants: updated guidelines from a National Heart, Lung, and Blood Institute working group. Circ Cardiovasc Genet. 2010; 3(6):574–580. [PubMed: 21156933]
17. Jarvik GP, Amendola LM, Berg JS, et al. for eMERGE Act-ROR Committee and CERC Committee; CSER Act-ROR Working Group. Return of genomic results to research participants: the floor, the ceiling, and the choices in between. Am J Hum Genet. 2014; 94(6):818–26. [PubMed: 24814192]
18. Reese PP, Hoo AC, Magee CC. Screening for sickle trait among potential live kidney donors: policies and practices in US transplant centers. Transpl Int. 2008; 21(4):328–31. [PubMed: 18086286]
19. Waits SA, Sung RS. Raising the Bar for Medically Complex Donors. Transplantation. 2014; 97(7): 730–1. [PubMed: 24521772]
20. Reese PP, Feldman HI, McBride MA, Anderson K, Asch DA, Bloom RD. Substantial Variation in the Acceptance of Medically Complex Live Kidney Donors Across US Renal Transplant Centers. Am J Transplant. 2008; 8(10):2062–70. [PubMed: 18727695]