Increasing the Supply of Kidneys for Transplantation by Making Living Donors the Preferred Source of Donor Kidneys

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Abstract: At the present time, increasing the use of living donors offers the best solution to the organ shortage problem. The clinical questions raised when the first living donor kidney transplant was performed, involving donor risk, informed consent, donor protection, and organ quality, have been largely answered. We strongly encourage a wider utilization of living donation and recommend that living donation, rather than deceased donation, become the first choice for kidney transplantation.

We believe that it is ethically sound to have living kidney donation as the primary source for organs when the mortality and morbidity risks to the donor are known and kept extremely low, when the donor is properly informed and protected from coercion, and when accepted national and local guidelines for living donation are followed.

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Abbreviation: ESRD = End-stage renal disease.

INTRODUCTION

Transplantation cures end-stage renal disease, and the only limitation to curing many more patients, some of whom die on the waiting list, is the lack of available organs. More than 100,000 patients require a kidney transplant, but the number of deceased donors has not risen to match the demand.1,2 The gap between potential recipients and organs available could be addressed either by listing fewer patients or by increasing the supply of donor organs. Limiting access is not acceptable since any change in this direction would affect well-established listing indications. There would be strong resistance from patients and doctors, if we attempted to exclude individuals from the waiting list for kidneys based on age, race, level of illness, or the etiology of kidney failure. Efforts to increase organ availability using deceased donors have been minimally effective, and the limited success has been achieved only by reducing the quality of the organs accepted for transplantation. Various proposals to increase the number of deceased donors, including presumed consent, reimbursement to donor families, use of donors after cardiac death, and more liberal criteria for donor acceptance, have not substantially increased the existing number of deceased donors.

To address these problems, we propose that living kidney donation, rather than deceased donation, becomes the first and preferred choice of patients and transplantation physicians for the treatment of end-stage renal disease (ESRD). We would recommend that living kidney donation be encouraged and promoted by the government and the transplantation community. The principal reasons for increasing the use of living kidney donors are as follows: the gap between supply and demand for organs continues to grow, that living kidney donors represent a much larger potential source of organs (possibly even in the millions) than deceased organ donors, and the outcomes of living donor kidney transplantation are significantly better than the ones of deceased organ transplantation. The maximum numbers of deceased organ donors have previously been estimated to be 12,000 to 15,000 per year.3 In the last decade, however, the number of living donors has decreased and that number remains below 6000 per year. Almost all of these donations are from family members.4

What are the barriers to increasing the availability of living unrelated donors? These barriers include the unwillingness of donors to give an organ to strangers and the general reluctance of healthy people to accept health risks and undergo surgery and anesthesia to benefit others.5 We believe a further reason why the number of living donations is not increasing relates to the ambivalence within the transplantation community about whether living donation is ethical. Dr Francis Moore, in whose program in 1954 the first successful kidney transplant was performed using a living donor, highlighted this ambivalence toward living donors when he wrote in 1964: “Is it ever morally right and ethically acceptable to injure one person to help another?”6,6

Because of these persistent ethical concerns, the prevailing consensus view in the transplantation community has been that living donation should be a second choice and should be considered only when no deceased organs are readily available or when there is an almost zero incidence of donor complications and a very low risk of mortality. A corollary is that living donation should never be openly promoted ahead of deceased donation but instead should be used as a last resort and often only if the donor volunteers without encouragement from the transplantation team. We believe the time has come to rethink this strategy of relying on deceased donation, an approach which is not meeting the increasing demand for kidney transplantation. Before we can move to the alternative strategy of encouraging living kidney donation, we must consider again the central question. Is it ethical to use living unrelated kidney donors as the principal source of kidneys for transplantation? And further, is it ethical to promote the use of living kidney donors?
These questions must be addressed in light of our current knowledge and experience. First, we must note the high rate of success in kidney transplantation. Further, living kidney donation is practiced widely in North America, Europe, and especially in Asia where deceased donation is not heavily relied upon. Since 1954, we estimate that more than 250,000 living kidney transplants have been performed in more than 30 countries. No country in the world prohibits the use of living donors in organ transplantation. This suggests that after 60 years, living kidney donation has been accepted on ethical grounds and on legal grounds by all of the world’s medical systems and societies. Nevertheless, as we noted, living donation continues to be regarded by most Western world centers, especially in Europe, as a second choice (except in Asia) compared to deceased organ donation.

It is also clear that the lack of enthusiasm for living donation is not related to the benefits from the procedure. In almost all cases, living kidney donation is the better clinical choice for recipients. In fact, the superior benefits of living compared to deceased donation are clear and proven. These benefits include decreased waiting time, better graft quality, the almost complete absence of the risk of disease transmission, the elective nature of the surgery, and most importantly, substantially better organ and recipient survival. According to data from the Scientific Registry of Transplant Recipients, the half-life of a kidney from a living donor is, on average, about 10 years longer than that of a kidney from a deceased donor. It is striking that deceased donor kidney transplantation is perhaps the only treatment we currently offer that has a demonstrated worse outcome than an alternative available therapy, living donor kidney transplantation.

Donor Risk

For those who continue to question the ethics of living donation, the central issue is donor risk. As Dr Thomas Starzl wrote in 1985 commenting on the then high reported rate of complications: “In view of such clinical information, is it ever ethical to encourage relatives to donate organs?” Since the first successful living donor kidney transplant in 1954, donor risks have decreased as donor nephrectomy has evolved from an open procedure to a laparoscopic procedure, as anesthesia and pain management have improved, and as safety measures for the donor have been regulated and implemented. In addition, donor coercion has decreased as informed consent and the use of donor advocates have become standards of care, and clinical outcomes have improved as data on donor morbidity and mortality have become publicly available.

Mortality

Mortality is the most feared complication from the act of donation. Based on data from the Scientific Registry of Transplant Recipients, among 27,850 US living kidney donors between 2007 and 2011, 32 (0.11%) died within 2 years of donating. Twelve of these deaths were attributed to medical reasons, 8 to suicide, 6 to homicide or accidental death, 4 to malignancy, and 2 from unknown causes. It seems reasonable to exclude the deaths due to malignancy and homicide/accidents—and possibly suicide as well. With these exclusions, the incidence of mortality in living kidney donors decreases to 0.05%. Whether the deaths from suicide are related to the act of donation would require a careful analysis of the clinical and psychiatric history of these donors before and after donation.

In a study published in 2010, Segev et al showed an even lower incidence of mortality among living donors: 0.03% in a population of 80,347 individuals with a median follow-up of 6.3 years. This mortality incidence was similar to that of a matched cohort of 9364 healthy individuals. The mortality rate in living organ donation is comparable to that of liposuction or scuba diving, both of which have a mortality of about 0.02%. While the mortality risk for living donors is not zero, it is low enough that the public, government regulators, and the professional community in every country have found the risk acceptable.

Morbidity

Immediate and long-term post-operative complications are the two components of donor morbidity risk. There is consistency in the reported incidence and type of perioperative and early post-operative morbidity. In a large, multi-center US study analyzing 3074 donors, major complications such as intra-operative injuries, pneumothorax, pulmonary embolus, myoccardial infarction, acute renal failure, rhabdomyolysis, and congestive heart failure were reported in 4.2% of donors and minor complications in 6.4%. These data are very similar to those from large studies in Norway and Japan and single-center studies in the US.

For long-term morbidity, the most essential component is the number of living donors who develop end-stage renal disease and require chronic dialysis or a kidney transplantation. Specifically, is the number of ESRD cases greater than would be expected from an age- and disease-matched cohort? Until very recently, the answer to this question was no. However, a recent publication compared the risk of ESRD in 96,000 kidney donors with the risk in a healthy cohort of 93,000 non-donors. This recent study found an estimated lifetime risk of ESRD to be 6.5 times higher in donors than in non-donors. The paper concluded that kidney donors had an increased relative risk of ESRD although the magnitude of the absolute increased risk remained small, from 14 per 10,000 in healthy non-donors to 90 per 10,000 in healthy donors to 326 per 10,000 in unscreened non-donors.

Methodological problems with the study were commented on by Gill and Tonelli who concluded: “The findings by Muzzaele and colleagues demonstrating the low absolute risk of ESRD, also an analysis of donors in the US, should reassure future donors of the safety of living kidney donation. It is known that focusing on relative increases in risk (rather than absolute increases in risk) can unduly influence treatment decisions, especially for rare outcomes. Given the limitations of the comparative analysis in the study by Muzzaele et al, it would be prudent for clinicians to emphasize the absolute risk of ESRD in discussions with prospective living donors, ideally using a decision aid that will facilitate the process of obtaining informed consent.” The other components of long-term morbidity after donation include the risk of developing hypertension, diabetes, or other health issues. Several studies indicate that when the donor is carefully selected and existing morbidities, including high blood pressure, higher body mass index, or family history of renal disease, are firm exclusion criteria, the risk of developing any significant life-altering health problem is not different from that of any age-matched non-donor individual.

Other long-term studies raise the question of possible increase in cardiovascular risk and end-stage renal disease when different control groups are chosen. On the other hand, there is growing and clear evidence that hypertension, proteinuria,
diabetes, and lower post-donation glomerular filtration rate are more common in African-American donors and in donors with a body mass index >30 kg/m² or with existing glucose intolerance.24

The studies cited in this paper support the view that in a properly selected donor, the quality of life and long-term health are not greatly affected by the act of donation. Living donation is not associated with zero mortality but with an extremely low mortality and is not associated with no increased risk of ESRD but with a small absolute risk of ESRD in kidney donors. Living kidney donation remains reasonably safe when strict donor selection criteria are applied.

Questions have been raised about whether African-American donors had a higher risk of ESRD than white donors. The recent paper cited above, by Muzala and his colleagues, reached the following conclusion: “This difference in ESRD was observed in both black and white individuals, with an estimated risk of 74.7 per 10,000 versus 23.9 per 10,000 black non-donors and an estimated risk of 22.7 per 10,000 white donors versus 0.0 white non-donors.”18

Additional Reasons for Using Living Donors

In addition to recipient benefit, there are several other reasons that support living donor organ transplantation. Living donor transplantation may prove to be more cost-effective than deceased organ transplantation, by consistently providing immediate graft function and lower organ acquisition fees. The fact that a living donor kidney has significantly longer half-life will decrease the number of patients requiring retransplantation increasing the number of organs for first time recipients. Moreover, since kidney transplant becomes cost-effective compared to dialysis in the management of end-stage renal disease within 2 years of the transplant, the more kidney transplants performed, the greater the economic and clinical benefit for society.

An increase in living donor transplantation in the United States also might have positive global effects. Transplant tourism has deleterious effects on other countries’ health systems and has its own set of serious ethical issues. If the number of living donors increases in the US, the number of patients with end-stage renal disease who would seek surgical intervention outside the US would also decrease.25

Recommendations

We recommend re-examining the ethics of living donation so that we resolve our ambivalence and stop equivocating about its ethical acceptability. After 60 years of performing living kidney donor operations, and after more than a quarter of a million such operations, transplant centers around the world have affirmatively answered the question of whether they think living donor organ transplantation is ethical. We also recommend that Health Resources and Services Administration and United Network for Organ Sharing modify their policies, that generally do not openly promote living kidney donation and consider making living donation rather than deceased donation the preferred and encouraged choice.

We should now initiate measures to promote living donation and to recruit more unrelated organ donors. This could be done through national advertising campaigns and by providing ethically acceptable incentives for living donation, including, for example, paid time off during evaluation and recovery, insurance coverage for all donor-related expenses, and free annual checkups. These would be simple, ethically acceptable steps to make living donation more widely used, convenient, and affordable.

CONCLUSION

At the present time, increasing the use of living donors offers the best solution to the organ shortage problem. The clinical questions raised when the first living donor kidney transplant was performed, involving donor risk, informed consent, donor protection, and organ quality, have been largely answered, thanks to the work of many physicians and surgeons, medical organizations such as the American Society of Transplant Surgeons, and the federal government through the Centers for Medicare and Medicaid Services and the United Network for Organ Sharing. We acknowledge that for certain categories of living donors the long-term follow-up data are incomplete or inconclusive, for example, for certain African-American donors. In this regard, we suggest that these donors will not be accepted until proper prospective long-term studies are concluded.

We strongly encourage a wider utilization of living donation and recommend that living donation, rather than deceased donation, becomes the first choice for kidney transplantation. We believe that it is ethically sound to have living kidney donation as the primary source for organs when the mortality and morbidity risks to the donor are known and kept extremely low, when the donor is properly informed and protected from coercion, and when accepted national and local guidelines for living donation are followed.

REFERENCES

1. Grams ME, Chow EK, Segev DL, Coresh J. Lifetime incidence of CKD stages 3–5 in the United States. Am J Kidney Dis. 2013;62:245–252.
2. Schold JD, Segev DL. Increasing the pool of deceased donor organs for kidney transplantation. Nat Rev Nephrol. 2012;8:325–331.
3. Sheehy E, Conrad SL, Brigham LE, et al. Estimating the number of potential organ donors in the United States. N Engl J Med. 2003;349:667–674.
4. Scientific Registry of Transplant Recipients. http://www.srt.org [Accessed on October 31, 2013].
5. Mandelbrot DA, Pavlakis M. Living donor practices in the United States. Adv Chronic Kidney Dis. 2012;19:212–219.
6. Moore FD. New problems for surgery. Drugs that act on the cell nucleus affect the surgeon’s work on cancer and on transplantation. Science. 1964;144:388–392.
7. Eurotransplant Statistics Report Library. http://statistics.eurotransplant.org/ [Accessed on October 31, 2013]

8. Starzl TE. Will live organ donations no longer be justified? Hastings Cent Rep. 1985;15:5.

9. Segev DL, Muzaale AD, Caffo BS, et al. Perioperative mortality and long-term survival following live kidney donation. JAMA. 2010;303:959–966.

10. Grazer FM, de Jong RH. Fatal outcomes from liposuction: census survey of cosmetic surgeons. Plast Reconstr Surg. 2000;105:436–446.

11. http://www.alertdiver.com/?articleNo=230

12. Patel S, Cassuto J, Orloff M, et al. Minimizing morbidity of organ donation: analysis of factors for perioperative complications after living-donor nephrectomy in the United States. Transplantation. 2008;85:561–565.

13. Mjøen G, Øyen O, Holdaas H, et al. Morbidity and mortality in 1022 consecutive living donor nephrectomies: benefits of a living donor registry. Transplantation. 2009;88:1273–1279.

14. Nakajima I, Iwadoh K, Koyama I, et al. Nine-yr experience of 700 hand-assisted laparoscopic donor nephrectomies in Japan. Clin Transpl. 2012;26:797–807.

15. Leventhal JR, Paunescu S, Baker TB, et al. A decade of minimally invasive donation: experience with more than 1200 laparoscopic donor nephrectomies at a single institution. Clin Transpl. 2010;24:169–174.

16. Cherikh WS, Young CJ, Kramer BF, et al. Ethnic and gender related differences in the risk of end-stage renal disease after living kidney donation. Am J Transpl. 2011;11:1650–1655.

17. Ibrahim HN, Foley R, Tan L, et al. Long-term consequences of kidney donation. N Engl J Med. 2009;360:459–469.

18. Muzaale AD, Massie AB, Wang MC, et al. Risk of end-stage renal disease following live kidney donation. JAMA. 2014;311:579–586.

19. Gill JS, Tonelli M. Understanding rare adverse outcomes following living kidney donation. JAMA. 2014;311:577–579.

20. Lentine KL, Schnitzler MA, Xiao H, et al. Racial variation in medical outcomes among living kidney donors. N Engl J Med. 2010;363:724–732.

21. Ibrahim HN, Kukla A, Cordner G, et al. Diabetes after kidney donation. Am J Transpl. 2010;10:331–337.

22. Lentine KL, Segev DL. Health outcomes among non-Caucasian living kidney donors: knowns and unknowns. Transpl Int. 2013;26:853–864.

23. Mjøen G, Hallan S, Hartmann A, et al. Long-term risks for kidney donors. Kidney Int. 2014;86:162–167.

24. Taler SJ, Messersmith EE, Leichtman AB, et al. Demographic, metabolic, and blood pressure characteristics of living kidney donors spanning five decades. Am J Transpl. 2013;13:390–398.

25. Cohen IG. Transplant tourism: the ethics and regulation of international markets for organs. J Law Med Ethics. 2013;41:269–285.

26. Ross LF, Rubin DT, Siegler M, et al. Ethics of a paired-kidney-exchange program. N Engl J Med. 1997;336:1752–1755.