Unilateral Nephrectomy: The Adverse Effects of Live Kidney Donation

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During a small symposium in Jerusalem devoted to ethical and legal aspects of organ transplantation, one of the participants asked whether there are deleterious effects of live kidney donation. Since there still proved to be some differences of opinion between surgeons and nephrologists,[1] I was asked to briefly summarize the "state of the art" of the consequences (long-term) of losing one healthy kidney.

It is universally accepted that only individuals with two healthy kidneys (proven by a variety of invasive and non-invasive techniques) can donate a kidney. Recently, "old" age is less of an obstacle; kidneys from subjects older than sixty years have occasionally been used. Obviously, minors cannot donate an organ for transplantation, except in the case of identical twins and then only with due legal backing. Everyone also accepts that, as with any surgical intervention, there is a certain risk of morbidity and a very small danger of mortality – though not nil – involved in the surgery of the donor.

Upon reviewing the literature on kidney donation it seems to me that the dangers involved have been well delineated. I will briefly summarize the main findings.

The major question, of course, is whether there are long-term effects of living with one kidney instead of two. Obviously, the lack of a second kidney as a "backup" in case of trauma to the remaining kidney poses a certain risk. To the best of my knowledge this is not reflected in a higher premium for life insurance, a rather sensitive index of the dangers lying ahead. Having only one kidney may, however, cause certain restrictions in life, but only in regard to

1. Editor's note: See also M. Halperin, "Organ Transplants from Living Donors," pp. 407-426, this volume, and notes 1-3 on p. 407.

unusual professions or sports activities that are hardly important for the average individual in day-to-day life.

From a purely medical point of view, the best answer was given by Provoost and Brenner, the former a Dutch researcher in experimental pediatric surgery (kidney), and the latter a worldwide leader in nephrology (adult).[2] They discuss the long-term consequences of congenital, unilateral renal agenesis, as well as of unilateral nephrectomy for renal disease in children and adults and kidney donation for renal transplantation (in adults). For many of these categories there is now a follow-up of subjects for a period of up to fifty years. Since the first live kidney donation was only performed in 1954,[3] the follow-up period for renal donation by healthy adults is somewhat less.

Provoost and Brenner conclude that "the outlook – of living with a single kidney – is largely uneventful for several decades, though a minority of individuels may develop hypertension, proteinuria and a few exhibit substantial loss of renal function leading to chronic renal failure." Everyone seems to agree that there is an increased incidence of generally mild hypertension and of mild to moderate proteinuria after kidney donation, particularly in older persons.[4]

The issue of chronic renal failure is less clear. Brenner has developed a theory that the extra workload imposed on the remaining kidney leads to "hyperfiltration" of that kidney and ultimately to chronic renal disease. He continues to promote this sequence of events.

Though this is certainly true for several animal models, it is not yet clear if it is indeed found in humans. Saran *et al.,* for example, did not find adverse effects of prolonged compensatory "hyperfiltration" in seventy-five kidney donors followed for twelve to

2. A.P. Provoost, B.M. Brenner, "Long-term Follow-up of Humans with Single Kidneys: the Need for Longitudinal Studies to Assess True Changes in Renal Function," *Current Opin Nephrol Hypertens* 2 (1993): 521-26.
3. J.P. Merrill, J.E. Murray, J.H. Harrison, W.R. Guild, "Successful Homotransplantation of the Human Kidney between Identical Twins," *JAMA* 160 (1956): 277-82.
4. A. Ohishi, H. Suzuki, H. Nakamoto, H. Katsumata, K. Hayashi, M. Ryuzaki, *et al.,* "Status of Patients who Underwent Uninephrectomy in Adulthood more than Twenty Years Ago," *Am J Kidney Dis* 26 (1995): 889-97. E. Toronyi, F. Alfoldy, J. Jatay, A. Remport, M. Hidvegi, G. Dabasi, *et al.,* "Evaluation of the State of Health of Living Related Kidney Transplantation Donors," *Transpl Int* 11, suppl. 1 (1998): S57-S59.

thirty-one years after surgery.[5] Most renal transplant surgeons and nephrologists tend to agree, but at the same time they are well aware of the possibility, though rare, that chronic renal disease may occur after kidney donation. More detailed testing of renal function after unilateral nephrectomy is needed to further evaluate this latter possibility.

A short explanation is needed to summarize this additional material.

Under normal conditions, healthy kidneys do not work at their maximum capacity; there is a certain reserve that can be activated in times of stress. This so-called renal reserve capacity (RRC) of glomerular filtration rate (GFR) and or renal blood flow (RBF) can easily be tested by measuring renal function (creatinine or inulin and para-aminohippuric acid clearances) before and after protein loading by an acute high-protein meal (milk or meat) or the intravenous administration of amino acids. The difference between the basic and the stimulated clearance measurements denotes the RRC. A reduction in or the total loss of the normal RRC for GFR (±20%) is generally seen as indicative of renal functional impairment.[6]

In a recent study,[7] in whose publication I was intimately involved, thirty-seven children under sixteen years of age who had undergone uninephrectomy were carefully followed for thirty years. This included repeat measurements of renal function, blood pressure, and urine, with a single determination of RRC after ten to thirty years. During those years, creatinine and urea clearances remained unchanged, no proteinuria was found, and blood pressure remained normal for age and gender. The RRC remained unchanged for ten years but in the second and third decades a significant reduction was observed. This seems to indicate a vulnerability of the solitary kidney's renal function, which "may possibly lead to renal functional impairment with longer follow-up." Again,

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5. R. Saran, S.M. Marshall, R. Madsen, P. Keavey, J.S. Tapson, "Longterm Follow-up of Kidney Donors: a Longitudinal Study," *Nephrol Dial Transpl* 12 (1997): 1615-21.
6. J.P. Bosch, S. Lew, S. Glabman, A. Lauer, "Renal Hemodynamic Changes in Humans: Response to Protein Loading in Normal and Diseased Kidneys," *Am J Med* 81 (1986): 809-15.
7. B.M. Regazzoni, N.B. Genton, J. Pelet, A. Drukker, J.P. Guignard, "Longterm Follow-up of Renal Functional Reserve Capacity after Unilateral Nephrectomy in Childhood," *J Urol* 160 (1998): 844-48.

I emphasize that none of the usual tests revealed any renal dysfunction, even up to thirty years after unilateral nephrectomy. Ter Wee and colleagues strongly feel that the RRC "cannot be used to test the existence of maladaptive glomerular hyperfiltration in subjects with a single kidney."[8] Others have used the measurement (with inulin clearance) with considerable success.[9]

In conclusion, it should be clear that from a twenty- to fifty-year follow-up of a significant number of subjects after uninephrectomy, the adverse effects of a kidney donation are rather minimal and consist of mild to moderate proteinuria and slightly higher blood pressure than could be expected based on the social and genetic background of the kidney donor's general population and his or her age and gender. Renal functional deterioration has occasionally been observed in older subjects, particularly in those with pre-existing hypertension. The uninephrectomized subjects should live completely normal lives without dietary restrictions. They should, however, be followed from time to time with renal functional tests. The measurement of RRC may have prognostic significance, although the final verdict on its reliability and usefulness is not yet in.

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8. P.M. Ter Wee, A.M. Tegzess, A.J. Donker, "Pair-tested Renal Reserve Filtration Capacity in Kidney Recipients and their Donors," *J Am Soc Nephrol* 4 (1994): 1798-1808.
9. M.S. Englund, U.B. Berg, K. Arfwidson, "Renal Functional Reserve in Transplanted and Native Single Kidneys of Children and Adults," *Pediatr Nephrol* 11 (1197): 312-17.