Risks and Outcomes of Living Donation

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Abstract

Living donors supply approximately 40% of renal allografts in the United States. Based on current data, peri-operative mortality after donor nephrectomy is approximately 3 per 10,000 cases, and major and minor peri-operative complications affect approximately 3–6% and 22% of donors, respectively. Donor nephrectomy does not appear to increase long-term mortality compared with controls, nor to increase ESRD risk among white donors. Within the donor population, the likelihood of post-donation chronic renal failure and medical comorbidities such as hypertension and diabetes appear to be relatively higher among some donor subgroups, such as African Americans and obese donors, but the impact of uni-nephrectomy on the lifetime risks of adverse events expected without nephrectomy in these sub-groups is not yet defined. As national followup of living donors in the U.S. is limited in scope, duration and completeness, additional methods for quantifying risk among diverse living donors are needed. In addition to improved national collection of follow-up data, possible sources of information on donor outcomes may include focused prospective studies with carefully defined control groups, and database integration projects that link national donor registration records to other data sources. Given the growth and evolving characteristics of the living donor population, as well as changes in surgical techniques, tracking of short and long-term risks after living kidney donation is vital to support truly informed consent and to maintain public trust in living donation. The transplant community must persist in efforts to accurately assess risk across demographically diverse living kidney donors.

Keywords

Hypertension; Kidney transplantation; Kidney failure; Living donors; Mortality; Postoperative complications; Risk

Living kidney donors reduce the growing gap between the demand for and supply of renal allografts, and offer their recipients the best opportunity for dialysis-free survival.1 Longer
waiting times for deceased donor transplants, recognition that even poorly-matched living donor kidneys provide good recipient outcomes, and increased use of minimally invasive surgical techniques for donor nephrectomy have stimulated growth in living kidney donation over the past 10 years. In the United States (U.S.), the number of kidney transplants from living donors increased from fewer than 2,000 in 1988 to 6,276 in 2010, when living donors supplied 37% of renal allografts nationally.

Despite increasing use of living donor organs to address the organ shortage, mandated follow-up of the health of living donors in the U.S. is limited in scope and duration. The Organ Procurement and Transplantation Network (OPTN) has collected follow-up data on living donors from participating transplant centers at six months and one year since 1999, including information such as serum creatinine, blood pressure and body mass index (BMI). Data on requirements for medications to treat hypertension and diabetes were added in 2004, and the duration of follow-up was extended to two years in 2008. These donor follow-up policies contrast with national tracking of solid organ transplant recipients by the OPTN for the life of the allograft. Even with this limited reporting period, missing data are common on living donor follow-up forms submitted to the OPTN. In 2006, complications data were more than 50% incomplete at one year and approximately one-third of living kidney donors were reported “lost to follow-up.” Emerging data also suggest that reporting rates are lower for donors who may have limited access to healthcare, such as those of non-white race or without health insurance.

In this context, much of the information on long-term outcomes after living donation has been drawn from single-center, retrospective studies. Recently, data integration methods involving linkage of the OPTN registry to other information sources such as the Social Security Death Master File (SSDMF) and health insurance claims have been applied as one method for capturing information on large samples of prior donors beyond the OPTN-mandated reporting periods. As the optimal approach to capturing and analyzing health outcomes after living kidney donation undergoes increasing debate among the transplant community and regulatory bodies, it is worthwhile to consider the state of available evidence. In this article, we review currently available information on peri-operative risks, long-term mortality, renal disease and medical outcomes after living kidney donation, and consider needs for ongoing and improved assessment of health outcomes among living donors.

Post-Operative Risks

According to OPTN reports for 51,113 living kidney donors in 1998–2008, 14 donor deaths (2.7 per 10,000) were reported by centers to the OPTN or identified in the SSDMF, and 39 donors (7.6 per 10,000) died within 12 months after donation. Recent linkage of OPTN registration data for 80,347 living donors in 1994–2009 with the SSDMF by Segev et al. yielded a similar 90-day mortality estimate of 3.1 per 10,000 that did not change significantly over the 15-year study period (Table 1A). Surgical mortality was higher in men than women (5.1 versus 1.7 per 10,000), black versus white and Hispanic donors (7.6 versus 2.6 and 2.0 per 10,000), and donors with versus without baseline hypertension (36.7 versus 1.3 per 10,000).
Early post-operative complications reported by centers to the OPTN within 6 weeks for 12,010 living donors in 2007–2008 indicated the need for blood transfusion in 0.4%, readmission in 2.1%, interventional procedures in 0.9% and re-operation in 0.5%. These are minimum estimates because more than 50% of source forms were submitted at less than 6 weeks after donation and because centers, rather than donors, are the source of the reporting. Records from the Nationwide Inpatient Sample (NIS), an all-payer inpatient care database comprising a stratified sample of 20% of non-federal U.S. hospitals from participating states, were also recently examined to quantify short-term complications after living donor nephrectomy. Based on discharge information for 9,437 patients who underwent donor nephrectomy in 1998 to 2006, the incidence of short-term complications considered major was 0.6%. The outcomes assessed were described as “common complications associated with high risk surgery” such as pulmonary compromise (0.2%), deep venous thrombosis and/or pulmonary embolism (0.1%), re-opening of the surgical site (0.1%), and gastrointestinal hemorrhage (0.1%), but the ascertainment algorithm was not further specified.

In contrast, higher post-operative complication rates have been reported with application of a standardized classification algorithm in other studies, including analyses of a prospective registry and of hospital coding data. The Clavien grading system defines surgical complications involving an array of systems including cardiac, respiratory, neurological, gastrointestinal, renal and other as “deviations from the ideal post-operative course”, and grades advancing severity by five levels according to treatment requirements. A prospective national registry capturing data for 1,022 living donor nephrectomies in Norway in 1997–2008 classified major complications as Clavien grade 3 events (i.e., requiring radiological or surgical intervention) or higher, and minor as Clavien grade 1 or 2 events. By this method, the incidence of major and minor complications was 2.9% and 18%, respectively. There were no deaths. Clinical correlates of a combined endpoint of major complications, perioperative bleeding, and/or intraoperative incidents included laparoscopic compared to open approach (adjusted odds ratio (aOR) 2.76), BMI >30 (aOR 1.76), right versus left kidney (aOR 1.59), and renal vessel anomalies (aOR 1.56). Higher risk with the laparoscopic approach was attributed to early generation equipment and the technical learning curve.

Application of the Clavien system to University HealthSystem Consortium hospital coding data for 3,074 living donation events at 28 U.S. centers in 2004–2005 identified an overall complications frequency of 10.6%, including major (Clavien grade >3) complications in 4.2%. Factors associated with increased risk of any complication included older donor age, obesity, tobacco use, and low center volume, although only annual center volume <50 donor nephrectomy procedures was associated with increased risk of major complications. A retrospective chart review of laparoscopic urological procedures including 553 donor nephrectomies in 1993–2005 at one high volume center reported major and minor Clavien complications frequencies of 5.8% and 22%, respectively.

Thus, in contrast with the relatively low frequency of complications within 6 weeks of donation identified by OPTN reporting, major complications in 3–6% and minor
complications in up to 22% during the nephrectomy hospitalization have been identified using the Clavien system.

These data highlight the importance of surveillance of post-operative complications after kidney donation by standardized methods such as prospective registries and/or coordinated assessments of hospital claims data using established grading systems. Attention to patients with higher risk clinical features, the impact of evolving surgical techniques, and the role of center experience and volume should be considered in the surveillance and evaluation of short-term complications after living donation.

Long-Term Mortality

As the OPTN collects living donor follow-up information for only two years, data on donor mortality beyond the peri-operative period has generally been drawn from retrospective, single-center studies that may be limited by loss to follow-up and selection biases. A recent cohort study of 3,698 donors at the University of Minnesota that achieved high ascertainment of long-term patient and renal survival status found no adverse impacts of living kidney donation on lifespan compared to general population life table estimates from the Human Mortality Database (Table 1A). This cohort was racially homogenous, with 98.8% white race participants. Linkage of OPTN and SSDMF records for a large, national living donor sample recently identified higher relative mortality over 12 years among older compared to younger donors, men versus women (HR 1.7, 95% CI 1.5–2.0), black versus white donors (HR 1.3, 95% CI 1.0–1.6) and donors with baseline hypertension (HR 1.7, 95% CI 1.1–2.9). However, long-term death rates did not exceed rates of matched control subjects from the National Health and Nutrition Evaluation Survey (NHANES).

The composition of reported deaths after kidney donation appears to differ from that in the general population. Cardiovascular disease (including stroke) comprises the leading cause of death in the general populations of many developed countries including the U.S. and Japan. In contrast, recent OPTN and SSDMF data identified cancer as the most common cause of death within seven years after kidney donation in the U.S., accounting for 10.3% of deaths overall and 23.8% of deaths with a reported cause. Among the 44% of deaths with reported causes, the next most common etiologies were cardiovascular disease (including heart attack, cerebral hemorrhage and aneurysm) in 14.0%, motor vehicle accidents in 14.0%, and other accidents in 12.5%. Malignancy was the attributed cause of 43% deaths after kidney donation in a recent study of long-term living donor outcomes at one transplant center in Japan that included causes for all identified deaths, followed by cerebrovascular disease in 11.3% and heart disease in 5.3%. The lower ranking of cardiovascular mortality among causes of donor may in part reflect effective screening and exclusion of potential donors with advanced or intermediate cardiovascular risk factors at evaluation. However, given the high frequency of unknown causes in >50% of the U.S. sample, better tracking of the details of post-donation mortality is warranted.

Chronic and End-Stage Renal Disease

Recent studies examining renal outcomes among living kidney donors are described in Table 1B. In addition to long-term ascertainment of donor mortality, end-stage renal disease
(ESRD) was assessed among the 3,698 living donors in the University of Minnesota cohort by reports of recipients and donors themselves. ESRD requiring dialysis or transplantation developed in 11 donors from this cohort at an average of 22.5+10.4 years post-donation, yielding a rate of 180 cases per million per year (PMPY), which did not exceed the national ESRD rate for white Americans of 268 cases PMPY. However, while only 45 of 3,698 donors in the full cohort were non-white, 3 of 11 donors who developed ESRD were non-white.

Assessment of renal function measures captured in the OPTN survey for donors in 2000–2005 at an average of 5 months post-donation found no appreciable differences in serum creatine or estimated glomerular filtration rate (eGFR) among African American compared with white donors in this early assessment period. In contrast, recent queries of kidney transplant candidate registrations raised concerns for racial disparities in ESRD risk in the longer term after living donation. While African Americans composed 12% of U.S. living kidney donors in 1996–2007, they represented 43% of 148 prior donors listed for kidney transplantation after donation. ESRD also appeared to develop within a shorter time from donation among affected black donors, with a median time to reporting of 16 years compared with 21 years in white donors who developed ESRD.

Lentine et al. recently linked OPTN records for 4,650 living donors, including 13% black and 8% Hispanic donors, with administrative claims of a private health insurer. Chronic kidney disease was indicated as a medical diagnosis in the claims among 5.2% of donors by the fifth donation anniversary. Diagnosed chronic kidney disease after nephrectomy was approximately twice as likely among black (aHR 2.32, P<0.05) or Hispanic (aHR 1.90, P<0.05) compared with white donors. Sub-analysis of donors who had benefits in the studied insurance plan after the introduction of stage-specific billing codes for chronic kidney disease indicated significantly increased risk of chronic kidney disease stage 3 or higher diagnoses among donors who were black (aHR 3.60, P = 0.009) or Hispanic (aHR 4.23, P = 0.006) compared with white donors. Chronic kidney disease requiring dialysis was reported in 2 of 271 black (0.7%, P=0.02 vs white) and 1 of 197 Hispanic (0.5%, P=0.10 vs white) prior donors, compared with no cases among 1786 white donors. The time from donation to ESRD ranged from 6.3 to 16.5 years. Provocative new research has identified coding variants in the apolipoprotein L1 (APOL1) gene that are strongly associated with nondiabetic ESRD risk in African Americans in an autosomal recessive pattern of inheritance, such that the presence of 2 risk alleles has been associated with marked increase in the risk of deceased donor allograft loss at one center. These data raise the possibility of genotyping as a future approach to risk stratify African American potential living donors. Outside the U.S., in a recent report of 8 donors at one center in Japan who developed CKD stage 5 or ESRD, the mean time from donation was 16 + 3.2 years. In most cases, renal function was stable for a prolonged period but then suddenly declined with new initiating events or comorbidities.

Recent analysis of 36 obese living kidney donors at the University of Maryland at 6.8+1.5 years after donation raises concern for hyperfiltration injury over time in this subgroup. At the follow-up evaluation, 47.7% had eGFR 30–59 ml/min/1.73 m², including six of seven (85.7%) obese donors who had microalbuminuria at follow-up. The absolute decrement in

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eGFR was also greater in African American obese donors, as compared with non-African American obese donors (33.3+9.6 vs 22.7+12.7 ml/min/1.73m$^2$, respectively; P=0.016).

Collectively, these data emphasize the relative insensitivity of short-term post-donation labs alone, and emphasize the importance of long-term donor follow-up methods to enable capture of renal complications that may develop over time after donation, particularly in higher risk groups such as African Americans, obese donors, or those with interval onset of comorbidities.

**Medical Outcomes**

Recent studies examining renal outcomes among living kidney donors are described in Table 1C. Data from predominantly white race cohorts suggest increased blood pressure levels and hypertension risk in prior donors compared with the general population, possibly due to physiological alterations (hyperfiltration in the remaining kidney, changes in vascular tone and renin-angiotensin-aldosterone regulation) and/or heightened follow-up. Meta-analysis of 48 studies involving 5,145 donors found 6 mmHg higher weighted mean systolic blood pressure and 4 mmHg higher weighted mean diastolic blood pressure in donors compared with controls after an average of seven years of follow-up, supporting an association of donation with a rise in blood pressure over that anticipated with normal aging. Based on linkage of Ontario organ procurement organization data for 1,278 living donors in 1993–2005 with provincial administrative health databases (92% white among those with reported race), Garg et al. found a higher incidence of claims-based diagnoses of hypertension among living donors compared with matched controls who were free of baseline comorbidity (16.3% versus 11.9%, HR 1.4, P<0.001). Emerging data raise concern for higher likelihood of medical comorbidity after donation in some subgroups, such as obese and non-white patients. Reese et al. found no differences in systolic blood pressure or eGFR changes from baseline to six months post-donation across donor BMI categories. In contrast, a high prevalence of hypertension of 41.6% was identified among 36 obese living donors assessed at an average of seven years post-donation at the University of Maryland.

Racial disparities in the burden and consequences of hypertension and diabetes among non-white racial and ethnic minorities in the general U.S. population are extensively documented but health outcomes among non-white donors has come to attention only recently. In the retrospective cohort study from the University of Minnesota, drug-treated hypertension and diabetes were reported in 25% and 3%, respectively, of 255 white donors assessed at an average of 12 years after donation. By contrast, several reports recently suggested higher frequencies of hypertension and diabetes among non-white kidney donors. Among a cohort of 38 Canadian Aboriginal donors evaluated at an average of 14 years after donation, 42% were hypertensive and 19% were diabetic compared with hypertension and diabetes in 14% and 2%, respectively, of Caucasian donor controls. Hypertension was identified in 41% of 39 African American donors studied at an average of seven years post-nephrectomy at one center in Maryland.
In a linkage of private insurance claims to OPTN living donor registrations, the estimated prevalence of diagnosed hypertension at five years after donation was 17.8%, and diabetes was indicated in 4.0%. Black donors, as compared with white donors, had approximately 50% increased relative risk of hypertension (aHR 1.52, P<0.05) and twice the relative risks of diabetes mellitus requiring drug therapy (aHR 2.31, P<0.05). Relative risks were similar for Hispanic compared to white donors. The estimated prevalence of diabetes at five years after donation did not exceed that in subgroups from NHANES defined by age, race and gender. However, the prevalence of hypertension after donation exceeded estimates from the NHANES in some subgroups, such as Hispanics.

These integrated administrative and registry data were also used to examine the association of recipient illness history, as a measure of family history, with post-donation hypertension and diabetes diagnoses. After adjustment for age, gender and race, recipient type 2 diabetes compared with non-diabetic recipient status was associated with more than twice relative risk of diabetes diagnosis in related donors (aHR 2.14, P=0.003). As compared with donors to related recipients with non-hypertensive ESRD, relatives of recipients with ESRD from hypertension had approximately 37% higher age and gender-adjusted relative risks of hypertension diagnosis after living kidney donation (aHR 1.37, P=0.009). Black donors were over-represented among related donors giving to recipients with hypertensive ESRD or with type 2 diabetes, and adjustment for race somewhat attenuated the associations of recipient hypertensive ESRD and of recipient type 2 diabetes with donor medical outcomes. However, the increased risk of post-donation hypertension and diabetes were not principally explained by race-related risk variation, as recipient illness history was significantly associated with the risk of these outcomes among white related donors.

Future work should seek to quantify implications of hypertension and diabetes after kidney donation for the risk of ESRD, cardiovascular disease, and other health outcomes that impact global health and quality of life. In the general population, each increase of 20 mm Hg usual systolic blood pressure (or, approximately equivalently, 10 mm Hg usual diastolic blood pressure) in mid-adulthood has been estimated to confer more than a two-fold difference in stroke-related mortality, and twice the risk of death from ischemic heart disease and other vascular causes. Diabetes confers approximately two-fold excess risk of an array vascular disease in the general population, independently from other conventional risk factors. However, the end-organ impact of hypertension and diabetes may differ in kidney donors because closer surveillance and early intervention in otherwise healthy adults may mitigate consequences. Nonetheless, better understanding of the risk for hypertension and diabetes is relevant to counseling on possible financial risks from future prescriptions, medical treatment and associated insurance premiums, and may strengthen policy proposals for provision of universal health insurance to living donors.

As end-organ damage from hypertension or diabetes generally develops after a latency, several authors have recently advanced the importance of considering expected lifespan and the lifetime risks of end-organ failure for the living donor. Based on lifetime risk patterns in the general population, Steiner estimated that some older donors with an isolated medical abnormality such as mild hypertension will face a similar or lower lifetime ESRD risk as that of young donors without baseline comorbidity who have an expected lifespan of more
than 50 years in which to develop end-organ complications. Based on a similar rationale, some programs such as the Mayo Clinic Kidney-Pancreas Transplant Program propose the “preferred living donor” as above the age of 50 at donation, as articulated in a recent Viewpoint by Textor. The Mayo Clinic program also defines less stringent acceptable upper boundaries for baseline blood pressure, blood glucose, body weight and kidney function with advancing age of the potential donor. Age-stratified donor selection based on baseline blood pressure is mentioned in the Amsterdam Forum clinical practice guidelines for the medical evaluation and care of the living donor, but other guidelines are not currently customized for demographic or other factors. Notably, as African American tend to donate at a younger average age and are more likely related to their recipient than white donors, demographic differences in lifetime risks may occur as a result of donation patterns. Attempts to delineate life-time risks of end-organ complications in relation to factors such as donor age, race, obesity and family history warrant ongoing attention.

**Pregnancy after Living Donation**

It is not uncommon for women of child-bearing potential to consider living kidney donation. Until recently, available pregnancy outcomes data in donors were largely limited to several small surveys and chart reviews. Two articles in 2009 addressed maternal and fetal outcomes after living kidney donation. Reisaeter et al linked the Norwegian Renal Registry with the Medical Birth Registry of Norway to assess pregnancies outcomes in kidney donors in 1967–2002. The authors identified 726 pregnancies among 326 donors, including 106 post-donation pregnancies. In unadjusted analyses, there were no significant differences in rates of gestational hypertension, preeclampsia, birth weights or infant survival among pregnancies occurring post-donation, pre-donation, or among a random sample from the birth registry. In a general liner model that adjusted for contributions of some mothers to more than one birth, as well as maternal age and parity, preeclampsia was more common in post-donation compared with pre-donation pregnancies (5.7% vs. 2.6%; P = 0.02). A large survey of donors at the University of Minnesota (1963–2007) captured responses for 822 donors with 2,426 pre-donation pregnancies and 223 donors with 459 post-donation pregnancies. In unadjusted analysis, post-donation as compared with pre-donation pregnancies were associated with a lower likelihood of full-term delivery (78.7% vs. 84.6%; P = 0.0004) and higher risks of fetal loss (19.2% vs. 11.3%; P < 0.0001), gestational diabetes (2.7% vs. 0.7%; P = 0.0001), gestational hypertension (5.7% vs. 0.6%; P < 0.0001), proteinuria (4.3% vs. 1.1%; P < 0.0001) and pre-eclampsia (5.5% vs. 0.8%; P < 0.0001). In women who had both pre- and post-donation pregnancies, this risk of adverse maternal outcomes was more likely to occur in their post-donation pregnancies (odds ratio 5.21). While these studies are limited by retrospective design and/or use of surveys, they support the need for continued study of the potential impact of donor nephrectomy on maternal and fetal outcomes. As both these studies captured dominantly white women, risks in other racial and ethnic groups are undefined.
Conclusion

Based on current data, peri-operative mortality after donor nephrectomy is approximately 3 per 10,000 cases, and major and minor peri-operative complications defined by the Clavien system affect 3–6% and 22% of donors, respectively. Donor nephrectomy does not appear to increase long-term mortality compared with controls, nor to increase ESRD risk among white donors. Within the donor population, the likelihood of post-donation chronic kidney disease, ESRD, and medical comorbidities such as hypertension and diabetes are relatively higher among some donor sub-groups, such as African Americans and obese donors, but the impact of uni-nephrectomy on the lifetime risks of adverse events expected without nephrectomy in these sub-groups is not yet defined. As national followup of living donors in the U.S. is limited in scope and duration, and barriers to the provision of donor follow-up such as cost inconvenience reduce the available information from mandated reporting, additional methods for quantifying risk among diverse living donors are needed. Several ongoing studies sponsored by the National Institutes of Health will report information on vital status, end-stage renal disease, renal function and comorbidities in selected donor cohorts, and increased support for national collection of longer-term follow-up data on all donors is the subject of active debate. Data integration involving linkage of the OPTN registry to other information sources such as national death records, CMS ESRD records and health insurance claims offer an additional method of data collection. Given the growth and evolving characteristics of the living donor population, as well as changes in surgical techniques, tracking of short and long-term risks after living kidney donation is vital to support truly informed consent and to maintain public trust in living donation. The transplant community must persist in efforts to accurately assess risk across demographically diverse living kidney donors.

Acknowledgments

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References


Table 1A
Summary of recent studies examining short- and long-term mortality among living kidney donors

<table>
<thead>
<tr>
<th>Reference</th>
<th>LKD Participants &amp; Data Source</th>
<th>Comparison Data (if any)</th>
<th>Outcome Measures</th>
<th>Findings Within LKD</th>
<th>Comparison of LKD and Non-LKD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrahim et al, N Engl J Med 2009 17</td>
<td>Retrospective cohort study of 3,698 LKD (98.8% white race) at one U.S. center in 1963–2007</td>
<td>• Age-and sex-specific life table estimates from the Human Mortality Database</td>
<td>• Death based on Social Security Death Master File (SSDMF) records up to December 2007</td>
<td>• 268 documented deaths</td>
<td>• LKD survival appeared similar to general population sample (statistical comparison not possible)</td>
</tr>
<tr>
<td>Segev et al, JAMA 2010 7</td>
<td>• Linkage of OPTN data for 80,347 U.S. LKD in 1994–2009 with SSDMF</td>
<td>• Sample from NHANES III, matched by age, gender, race, education, smoking history, BMI, and systolic blood pressure</td>
<td>• Surgical mortality (within 90 d) based on SSDMF records</td>
<td>• Surgical mortality: 3.1 per 10,000 LKD</td>
<td>• Long-term LKD mortality not higher vs age-and comorbidity-matched controls</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Long-term death (up to 12 yr) based on SSDMF</td>
<td>• Correlates of higher relative surgical mortality in LKD: male gender, black race, baseline hypertension</td>
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<tr>
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<td></td>
<td>• Correlates of higher relative long-term mortality in LKD: older age, male gender, black race, baseline hypertension</td>
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Table 1B

Summary of recent studies examining renal outcomes among living kidney donors

<table>
<thead>
<tr>
<th>Reference</th>
<th>LKD Participants &amp; Data Source</th>
<th>Comparison Data (if any)</th>
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<tr>
<td></td>
<td>OPTN data living donor registrations and transplant waitlist registrations in 1993–2005</td>
<td>N/A</td>
<td>Transplant waitlist registrations in prior LKD</td>
<td>44% of 102 LKD waitlisted after donation in the period were black</td>
<td>Black LKD comprised 14.3% of 8,889 LKD in the period, and were over-represented among LKD on the waitlist (P&lt;0.001).</td>
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<tr>
<td></td>
<td>Retrospective cohort study of 3,698 LKD at one U.S. center in 1963–2007</td>
<td>United States Renal Data System, annual ESRD incidence rates</td>
<td>ESRD based on report of the LKD or recipient</td>
<td>ESRD: 180 cases PMPY</td>
<td>ESRD in LKD did not exceed national ESRD rate for white Americans (268 cases PMPY)</td>
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<tr>
<td></td>
<td>Linkage of OPTN data for 4,690 LKD in 1987–2007 with administrative billing claims from a private health insurer (2000–2007 claims)</td>
<td>Median time from donation to end of insurance: 7.7 yrs</td>
<td>Claims-based diagnoses of CKD</td>
<td>CKD diagnosis: Overall, 5.2% at 5 yrs. Approximately twice as likely among black (aHR 2.32, P=0.05) or Hispanic (aHR 1.90, P=0.05) compared to white LKD</td>
<td>N/A</td>
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<tr>
<td></td>
<td>N/A for renal outcomes</td>
<td>Stage-specific coding examined a sub-group of 2,307 with insurance benefits after start of stage-specific coding</td>
<td>CKD stage 3 or higher in sub-analysis: more likely in black (aHR 3.60, P=0.009) or Hispanic (aHR 4.23, P=0.006) vs white LKD</td>
<td>Dialysis-requiring CKD in sub-analysis: 0.7% (P=0.02 vs white) and 0.5% Hispanic (P=0.10) LKD, vs 0 cases among white LKD</td>
<td>N/A</td>
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</table>
Summary of recent studies examining medical outcomes among living kidney donors

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<tr>
<td>Garg et al, Transplantation 2008 ¹⁰</td>
<td>• Linkage of Ontario organ procurement organization data for 1,278 LKD in 1993–2005 with provincial administrative health databases • Mean followup: 6.2 yrs</td>
<td>• Sample from the administrative data, free of baseline comorbidity and matched by age, sex, neighborhood income and frequency of non-physician visits</td>
<td>• Primary: Death or claims for major adverse cardiovascular event (MACE*) • Secondary: Hypertension diagnosis in claims</td>
<td>• Death or MACE: 1.3% in LKD • Hypertension: 16.3% in LKD</td>
<td>• No significant difference in LKD death or MACE vs control incidence of 1.7% (HR 0.7, P=0.22). • Diagnosed hypertension more frequent in LKD vs control incidence of 11.9% (HR 1.4, P&lt;0.001)</td>
</tr>
<tr>
<td>Ibrahim et al, N Engl J Med 2009 ¹⁷</td>
<td>• Subgroup of 255 (99.2% white) from cohort of 3,698 LKD at one U.S. center in 1963–2007</td>
<td>• Cross-sectional sample from NHANES 2003–2004, and 2005–2006 cohorts, matched by age, sex, race and BMI</td>
<td>• Hypertension: Use of antihypertensive drugs • Diabetes: Self-report</td>
<td>• Treated hypertension: 24.7% LKD • Diabetes: 3.5% LKD vs 5.9% controls (∗P=0.10)</td>
<td>• No difference in LKD hypertension vs control prevalence 28.8% (∗P=0.83) • No difference in LKD diabetes vs control prevalence 5.9% (∗P=0.10)</td>
</tr>
<tr>
<td>Lentine et al, N Engl J Med 2010 ⁸</td>
<td>• Linkage of OPTN data for 4,650 LKD in 1987–2007 with administrative billing claims from a private health insurer (2000–2007 claims) • Median time from donation to end of insurance: 7.7 yrs</td>
<td>• NHANES 2005–2006 cohort</td>
<td>• Claims-based diagnoses of hypertension or diabetes • Hypertension or diabetes requiring medical treatment based on pharmacy claims</td>
<td>• Hypertension: Overall, 17.8% at 5yr. 52% relative increase in black (aHR, 1.52, P&lt;0.05) and 36% relative increase in Hispanic (aHR 1.36, P&lt;0.05) vs white LKD • Drug-treated diabetes: more than twice as likely among black (aHR 2.74, P&lt;0.05) or Hispanic (aHR</td>
<td>• Prevalence of diabetes among all LKD at 5yrs did not exceed that in NHANES, but hypertension prevalence exceeded NHANES estimates in some subgroups</td>
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<td>1.24, <em>P&lt;0.05</em> vs white LKD</td>
<td>1.24, <em>P&lt;0.05</em> vs white LKD</td>
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BMI, body mass index; ESRD, end-stage renal disease; GFR, glomerular filtration rate; NHANES, National Health and Nutrition Examination Survey; PMPY, per million per year

*MACE defined as: myocardial infarction, stroke, or revascularization of a coronary, cerebral or peripheral artery*