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Perioperative Complications After Living Kidney Donation: A National Study

K. L. Lentine[1,*], N. N. Lam[2], D. Axelrod[3], M. A. Schnitzler[1], A. X. Garg[4], H. Xiao[1], N. Dzebisashvili[3], J. D. Schold[5], D. C. Brennan[6], H. Randall[1], E. A. King[7] and D. L. Segev[7]

[1]Center for Abdominal Transplantation, Saint Louis University School of Medicine, St. Louis, MO
[2]Division of Nephrology, University of Alberta, Edmonton, Alberta, Canada
[3]Division of Abdominal Transplantation, Department of Surgery, Dartmouth Hitchcock Medical Center, Hanover, NH
[4]Division of Nephrology, Western University, London, Ontario, Canada
[5]Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH
[6]Transplant Nephrology, Washington University School of Medicine, St. Louis, MO
[7]Division of Transplantation, Department of Surgery, Johns Hopkins School of Medicine, Baltimore, MD
**Corresponding author: Krista L. Lentine, lentinek@slu.edu*

We integrated the US transplant registry with administrative records from an academic hospital consortium (97 centers, 2008–2012) to identify predonation comorbidity and perioperative complications captured in diagnostic, procedure, and registry sources. Correlates (adjusted odds ratio, aOR) of perioperative complications were examined with multivariate logistic regression. Among 14 964 living kidney donors, 11.6% were African American. Nephrectomies were predominantly laparoscopic (93.8%); 2.4% were robotic and 3.7% were planned open procedures. Overall, 16.8% of donors experienced a perioperative complication, most commonly gastrointestinal (4.4%), bleeding (3.0%), respiratory (2.5%), surgical/anesthesia-related injuries (2.4%), and "other" complications (6.6%). Major Clavien Classification of Surgical Complications grade IV or higher affected 2.5% of donors. After adjustment for demographic, clinical (including comorbidities), procedure, and center factors, African Americans had increased risk of any complication (aOR 1.26, p = 0.001) and of Clavien grade II or higher (aOR 1.39, p = 0.0002), grade III or higher (aOR 1.56, p < 0.0001), and grade IV or higher (aOR 1.56, p = 0.004) events. Other significant correlates of Clavien grade IV or higher events included obesity (aOR 1.55, p = 0.0005), predonation hematologic (aOR 2.78, p = 0.0002) and psychiatric (aOR 1.45, p = 0.04) conditions, and robotic nephrectomy (aOR 2.07, p = 0.002), while annual center volume >50 (aOR 0.55, p < 0.0001) was associated with lower risk. Complications after live donor nephrectomy vary with baseline demographic, clinical, procedure, and center factors, but the most serious complications are infrequent. Future work should examine underlying mechanisms and approaches to minimizing the risk of perioperative complications in all donors.

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; ICD-9, *International Classification of Diseases, 9th Revision*; NIS, Nationwide Inpatient Sample; OPTN, Organ Procurement and Transplantation Network; UHC, University HealthSystem Consortium

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Introduction

During the past decade, kidney transplantation from living donors rose markedly, reaching a current rate in the United States of approximately 6000 live donations per year (1). The growth in living donation has been accompanied by changes in donor characteristics, including greater racial diversity, more unrelated donors (2), and increased donation from persons with baseline health conditions including obesity and hypertension (3,4). Early donor nephrectomy complications reported by centers to the Organ Procurement and Transplantation Network (OPTN) from 2000 to 2012 indicated the need for blood transfusion in 0.4%, vascular complications in 0.3%, and reoperation in 0.5% (5). These frequencies are substantially lower than estimates of 3–6% for major complications and 18–22% for minor complications identified in a prospective Norwegian donor registry and US hospital records (6,7), supporting a need to expand collection of perioperative complications with other information sources.

Using data from the Nationwide Inpatient Sample (NIS), Schold et al identified a sample of US living kidney donors from 1998 to 2010 based on the *International Classification of Diseases, 9th Revision* (ICD-9) diagnosis and procedure codes (8). Procedure-related complications were reported after 7.9% of donations and were more common among men, Medicare beneficiaries, and those with hypertension. Limitations of this study include the lack of confirmation of donor status through patient-level

linkages to the OPTN registry and use of weighting schemes to draw inferences for a "represented" sample of all US donors based on a stratified sample of 20% of acute care hospitalizations (9). The reported perioperative mortality was 0.17%, which, while low, is >5 times greater than 90-day mortality estimates generated from OPTN reports or linkage of the OPTN registry to national death records (10,11). This suggests that some patients who underwent nephrectomy for clinical indications unrelated to donation were inadvertently included. The study also lacked information collected in the OPTN such as details of the surgical procedure (e.g. laparoscopic or open approach) and transplant center donor nephrectomy volume. Finally, the outcome of interest was defined by "procedure-related complication" codes but did not include other diagnoses or procedures, and perioperative complications were not classified in terms of severity or involved organ systems.

In a smaller study, Patel et al examined the University HealthSystem Consortium (UHC) to study perioperative complications in 3074 living kidney donors from 28 US centers during 2004 and 2005 (12). The UHC is an alliance of 107 academic medical centers and 234 of their affiliated hospitals (approximately 90% of the nation's nonprofit academic medical centers) that captures administrative data submitted on UB-04 billing forms, including patient demographics and ICD-9 codes. As in the study by Schold et al, diagnostic and procedure codes were used to identify living kidney donors, their comorbidities, and perioperative complications. In addition, Patel et al categorized complications by using a modified Clavien Classification of Surgical Complications system, although details of included diagnosis and procedure codes were not provided. In this study, the overall complication rate was 10.6% and more severe complications (Clavien grade III or higher) were identified in 4.2% of cases. Limitations of this study include small sample size, description of an earlier era, and lack of patient-level linkage with the OPTN registry to confirm donor status and provide information such as surgical technique and side of nephrectomy.

In the current study, we combined the value of confirmed donor status and baseline donor and procedure characteristics recorded in the OPTN registry with more-detailed descriptions of predonation comorbidity and perioperative complications captured in hospital administrative records. Our goal was to use this novel data source to advance understanding of the frequency, severity, and correlates of perioperative complications after live donor nephrectomy in US contemporary practice.

Methods

Data sources and sample

We conducted a retrospective study by linking transplant registry and healthcare databases in the United States to determine baseline characteristics, covariate information, and outcome events for live kidney donations in 2008–2012. This study used the OPTN, which includes data on all donors, waitlisted candidates, and transplant recipients in the United States, submitted by the members of the OPTN, and which has been described elsewhere (13). The Health Resources and Services Administration, US Department of Health and Human Services provides oversight to the activities of the OPTN contractor.

Presumptive living kidney donors were drawn from the UHC database by extracting records for patients with a primary diagnosis of kidney donation (ICD-9 code V59.4) and a primary procedure of nephroureterectomy (ICD-9 code 55.51) (Table S1). In contrast to previous studies (8,12,14), live donor status was confirmed by linkage to the OPTN registry, using transplant center, date of donation, and donor age and sex. Residential ZIP codes were available for verification of duplicate matches (no duplicates were identified for this sample). All direct identifiers were removed before the final data set was available for analysis.

Analyses were performed by using Health Information Portability and Accountability Act–compliant limited datasets, with all direct identifiers removed. Because of the large sample size, the anonymity of the patients studied, and the nonintrusive nature of the research, a waiver of informed consent was granted per the Department of Health and Human Services Code of Federal Regulations (Title 45, Part 46, Paragraph 46.116). The study was approved by the Saint Louis University Institutional Review Board.

Covariate information

Figure 1 and Table S1 summarize information for the study covariates including the source databases, definitions, ICD-9 codes, and sample frequencies. Baseline donor demographic and clinical information ascertained for living kidney donors from the OPTN at the time of donation included age, sex, race, donor–recipient relationship, presence of health insurance, body mass index (BMI), physical limitations, hypertension (defined as a reported condition, use of medication, systolic blood pressure ≥140 mmHg, or diastolic blood pressure ≥90 mmHg), and history of smoking as reported by the transplant center. Baseline comorbid conditions were also extracted from UHC diagnosis codes indicated as "present on admission" including supplementation of OPTN-reported obesity, hypertension, and smoking; additional clinical conditions were categorized by organ system. Intended procedure type (laparoscopic or open) and side of nephrectomy (left or right) were identified from the OPTN registry; further characterization of robotic-assisted nephrectomy procedures was based on ICD-9 procedure codes from the UHC database. The payer for donation (which in the US health system is the recipient's insurance) was classified as private, Medicare, or other per UHC reports. Average annual live donor nephrectomy volume for the included centers was characterized in approximate tertiles as ≤10, 11–50, and >50 per year.

Ascertainment and classification of perioperative complications

Perioperative complications were identified from ICD-9 diagnostic and procedure codes reported to UHC during the nephrectomy hospitalization; vascular complications, conversion to open nephrectomy, reoperations, death, and other complications reported to the OPTN at discharge, as well as intensive care stay and death reported to the UHC, were also included (Table S1). Indication of a complication in any source was counted as an event. Postoperative complications were classified by organ system/type, and severity grading was performed according to an adaption of the Clavien Classification of Surgical complications, which defines complications as deviations from the ideal postoperative course and grades these events according to the level of treatment needed (15,16). Complications were analyzed by category at the patient level. We considered severity of complications in terms of the highest-grade

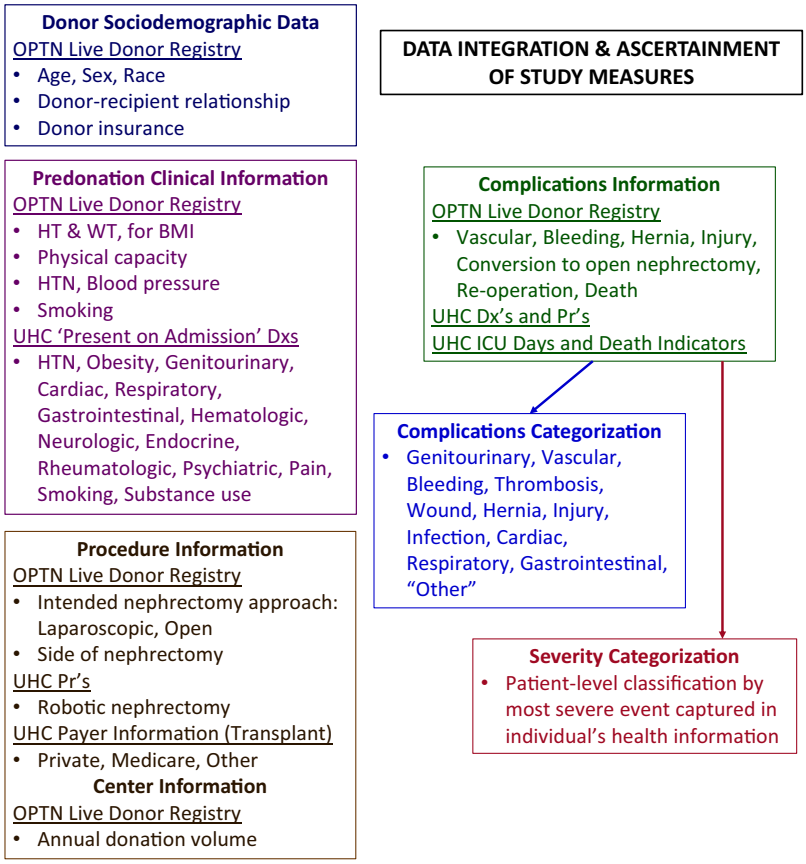

Figure 1: Data integration to capture baseline donor characteristics, procedure information, and perioperative complications. BMI, body mass index; Dx, diagnosis; HT, height; HTN, hypertension; ICU, intensive care unit; OPTN, Organ Procurement and Transplant Network; Pr, procedure; UHC, University HealthSystem Consortium; WT, weight.

complication reported for each patient as exceeding thresholds of grades II, III, and IV successively, wherein grade II included transfusions, grade III indicated requirements for reoperation, endoscopic, or radiological interventions, grade IV indicated life-threatening complications including requirement for intensive care, single-organ failure (e.g. need for dialysis, mechanical ventilation), or multiorgan failure; and grade V reflected patient death (Table S1). Patients categorized as experiencing grade I complications had a complication diagnosis but lacked indication of treatments denoting a higher severity level. All complication classification (percentage agreement 96.8%, κ concordance 0.96) and Clavien grading (percentage agreement 96.6%, κ concordance 0.95) was performed independently by two physicians (K.L.L., E.A.K.) based on review of diagnostic and procedure codes in isolation (without any associated patient information); disagreements were adjudicated by a third physician (D.L.S.).

Statistical analyses

Data sets were merged and analyzed with SAS (Statistical Analysis Software) version 9.4 (SAS Institute Inc., Cary, NC). In all outcome analyses, we interpreted two-tailed p-values as <0.05 as statistically significant. Associations (adjusted odds ratio [aOR]) of donor demographic factors with categories of baseline comorbidity were examined by multivariate logistic regression. Logistic regression was also used to determine independent associations of donor demographic and clinical factors, as well as procedural and center characteristics, with occurrence of any perioperative complication and complications exceeding Clavien severity thresholds. In secondary analyses, we examined associations of donor demographics (forced inclusion) and clinical factors with types of complications. Due to lower frequencies of individual complication categories, stepwise selection was performed across characteristics aside from demographics, with retention of factors based on $p < 0.05$ for associations of any level of the factor with the complication of interest.

Results

Baseline characteristics of the living kidney donor sample

Of 15 587 patients identified in the 97-center UHC sample with live donor diagnosis and nephrectomy procedure codes between September 2008 and December 2012, 96% (14 964) were verified as live donors through linkage with the OPTN registry. The baseline characteristics of these patients were similar to that of all US living kidney donors during the same period (Table S2). Among the study population, 72.6% were white, 11.6% were African American, 10.9% were Hispanic, and 4.9% were of other races (Table 1). The mean age at the time of donation was

42.1 years (standard deviation 11.8) and 61.7% were female; 52.8% were biologically related to their recipient. Nephrectomy procedures were predominantly laparoscopic (93.8%); 2.4% were robotic and 3.7% were planned open procedures. Twelve percent of donors had predonation hypertension; other baseline comorbidities included endocrine disorders in 11.8%, gastrointestinal conditions in 8.1%, psychiatric disorders in 7.3%, and genitourinary conditions in 2.0% (Table 1; see Table S1 for conditions included in baseline comorbidity categories). Seventeen percent of donors had reported obesity (BMI $\geq$30 kg/m^2, although information on BMI was missing in 18.5%), and 8.9% had a smoking history.

Correlates of baseline comorbidity

After multivariate adjustment, each increase in year of donor age was associated with a 5–7% higher likelihood of hypertension, genitourinary conditions, and cardiac conditions at the time of donation (Table S3). Female donors were approximately 50% less likely to have hypertension and genitourinary conditions at baseline but more than twice as likely to have hematologic disorders, psychiatric disorders, and pain disorders. Compared with white donors, African American donors in the study period had more common predonation hypertension (aOR 1.22, $p = 0.02$), hematologic (aOR 4.76, $p < 0.0001$) and neurologic (aOR 2.19, $p = 0.03$) conditions, but less endocrine (aOR 0.47, $p < 0.0001$) and psychiatric (aOR 0.25, $p < 0.001$) comorbidity. Obese donors were more likely to have hypertension (aOR 1.47, $p < 0.001$), respiratory conditions (aOR 1.74, $p < 0.0001$), gastrointestinal disorders (aOR 1.41, $p < 0.0001$), and endocrine disorders (aOR 1.46, $p < 0.0001$) compared with nonobese donors. The most recent donors (2011–2012) were 30% less likely to have genitourinary diseases or cardiac disorders compared with donors from earlier in the study (2008–2010) but had a similar prevalence of hypertension.

Correlates of perioperative complications by severity

Overall, 16.8% of donors experienced a perioperative complication, including Clavien grade II or higher in 8.8%, Clavien grade III or higher in 7.3%, and Clavien grade IV or higher in 2.5%. Compared with white donors, African American donors experienced higher rates of any complication (18.2% vs. 15.5%, $p = 0.005$) as well as complications exceeding progressive severity thresholds including Clavien grade IV or higher (3.7% vs. 2.2%, $p = 0.0002$) (Figure 2). After adjustment for other demographic and clinical factors, compared with white donors, African Americans were more likely to experience any perioperative complication (aOR 1.26, $p = 0.001$) and Clavien grade II or higher (aOR 1.39, $p = 0.0002$), Clavien grade III or higher (aOR 1.56, $p < 0.0001$), and Clavien grade IV or higher (aOR 1.56, $p = 0.004$) events.

The relative likelihood of any perioperative complication rose by 1% with each increase in year of donor age (aOR 1.01, $p < 0.0001$) (Table 2). Women were 14% less likely to experience any perioperative complication postdonation (aOR 0.86, $p = 0.001$). Obese donors were 55% more likely to experience the most severe perioperative complications (aOR 1.55, $p = 0.0005$). Predonation hypertension was not associated with increased risk of any perioperative complication. However, predonation genitourinary conditions (aOR 1.92, $p < 0.0001$), hematologic disorders (aOR 1.60, $p = 0.003$), and psychiatric diagnoses (aOR 1.29, $p = 0.002$) were associated with increased risk of a perioperative complication as well as with more severe complications (aOR 2.62, $p < 0.001$ for Clavien grade III or higher events in those with genitourinary conditions; aOR 2.78, $p = 0.002$ and aOR 1.45, $p = 0.04$, for Clavien grade IV or higher events in those with hematologic and psychiatric disorders, respectively). Donors who underwent planned open nephrectomy were 31% more likely to experience any perioperative complication (aOR 1.31, $p = 0.02$) compared with donors who underwent laparoscopic nephrectomy. Donors who underwent robotic nephrectomy were twice as likely to experience severe perioperative complications (aOR 2.07, $p = 0.002$ for Clavien grade IV or higher events). Transplantation at centers with the highest annual volume of living donor nephrectomies was associated with reduced risk of any perioperative complication (aOR 0.56, $p < 0.0001$) and of the most severe complications (aOR 0.55, $p < 0.0001$ for Clavien grade IV or higher events). Compared with donations in 2008–2010, donors who underwent nephrectomy in 2011–2012 were modestly more likely to experience any perioperative complication (aOR 1.13, $p = 0.007$) and had increased risk of more severe complications (aOR 1.69, $p < 0.0001$ for Clavien grade IV or higher events).

Correlates of categories of postdonation perioperative complications

Overall, the most common types of perioperative complications were gastrointestinal (4.4%), bleeding (3.0%), respiratory (2.5%), and surgical/anesthesia-related injuries (2.4%); "other" complications were identified in 6.6% (Table S1). Among the sample, 2.4% required intensive care and in-hospital mortality was 0.007%. Compared with white donors, African American donors had higher frequencies of complications related to genitourinary, vascular, bleeding, hernia, injury, infection, respiratory, gastrointestinal, and other types of disorders, although event counts by specific complication type were low and unadjusted differences were generally not statistically significant (Figure 3). However, after adjustment for other baseline donor, procedure and center factors, African American donors were more likely to experience vascular complications (aOR 1.80, $p = 0.03$), hernias (aOR 1.77, $p = 0.02$), gastrointestinal complications (aOR 1.46, $p = 0.004$), and other complications (aOR 1.37, $p = 0.04$) (Table S4). Other significant correlates of complication types included age and sex. Each increase in

Table 1: Baseline characteristics of the sample of living kidney donors by race

Baseline characteristics	Full cohort (N = 14 964)	White (n = 10 858)	African American (n = 1736)	Hispanic (n = 1628)	Other races (n = 742)
Age at donation, years	42.1 (11.8)	43.7 (11.6)	37.7 (10.9)‡	37.5 (10.9)‡	39.6 (11.6)‡
Female	61.7	62.2	59.3*	60.1	64.2
Donor–recipient relationship			‡	‡	‡
First-degree relative	45.2	40.6	57.7	59.0	53.8
Other biological relative	7.6	7.3	10.1	7.9	6.3
Unrelated	47.2	52.1	32.2	33.1	39.9
Donor health Insurance			‡	‡	‡
Insured	73.1	76.4	63.9	61.9	69.4
Uninsured	11.6	9.7	15.0	19.0	15.2
Missing	15.4	13.9	21.1	19.1	15.4
Body mass index, kg/m^2			‡	‡	‡
<18.5	1.3	1.2	1.3	0.8	2.6
18.5 to <25	30.5	30.9	25.1	27.2	45.6
25 to <30	32.2	32.0	32.4	36.0	26.8
≥30	17.4	16.5	25.9	19.0	8.5
Missing	18.5	19.4	15.3	17.0	16.6
Physical capacity			†	‡	*
No limitations	96.2	95.5	97.6	98.8	96.9
Limitations	0.4	0.4	0.4	0.2	0.8
Missing	3.4	4.1	2.1	1.0	2.3
Comorbid conditions					
Hypertension	12.2	13.0	12.3	7.7‡	10.4*
Genitourinary	2.0	2.3	1.3*	0.9†	1.6
Cardiac	0.9	1.1	0.6	0.3*	0.8
Respiratory	5.5	5.6	6.1	4.6	4.0
Gastrointestinal	8.1	9.1	6.0‡	5.3‡	5.0†
Hematologic	1.6	1.2	4.8‡	1.3	1.4
Neurologic	0.3	0.3	0.6*	0.1	0.4
Endocrine	11.8	13.1	5.0‡	7.2‡	9.0†
Rheumatologic	0.2	0.2	0.2	0.2	0.3
Psychiatric	7.3	9.2	2.3‡	2.3‡	2.7‡
Pain	3.3	3.6	3.0	1.9†	2.8
Smoking	8.9	9.5	10.0	5.0‡	6.9*
Other substance use	0.7	0.6	1.2*	0.6	0.4
Procedure and center characteristics					
Nephrectomy type, intended			‡	‡	*
Laparoscopic (nonrobotic)	93.8	94.9	89.4	91.3	93.5
Laparoscopic (robotic)	2.4	1.3	5.5	6.5	3.0
Open	3.7	3.7	5.1	2.2	3.5
Side of donated kidney					
Left	86.3	85.8	87.8*	87.7*	86.7
Right	13.7	14.2	12.2	12.3	13.3
Payer for donation			†		*
Commercial	29.5	30.1	27.0	28.6	28.6
Medicare	13.7	13.0	16.1	14.8	16.4
Other	56.8	56.9	56.9	56.6	55.0
Average annual center volume			*	‡	
≤10	1.8	1.4	2.3	3.8	2.4
11–50	41.3	42.3	41.3	34.9	41.4
>50	56.8	56.3	56.5	61.3	56.2
Donation year			*		
2008–2010	55.3	55.1	57.9	53.8	55.5
2011–2012	44.7	44.9	42.1	46.2	44.5

Data presented as percentages (%) except for age, which is presented as mean (standard deviation).
The χ^2 comparison of trait distributions within each race compared to white donors: *p < 0.05–0.002, †p = 0.001–0.0001, ‡p < 0.0001.

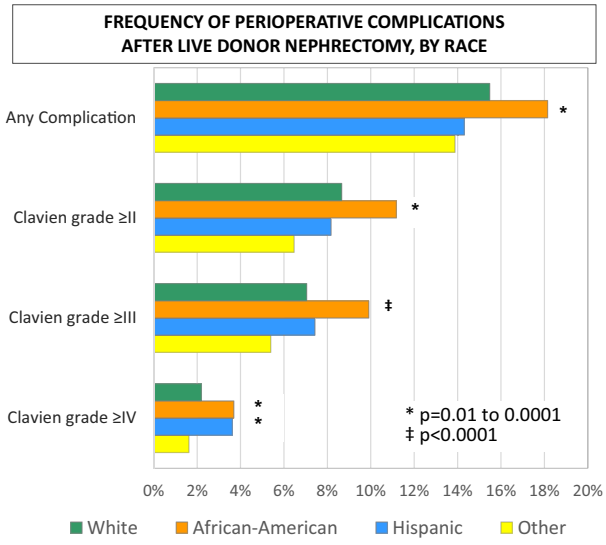

Figure 2: Frequencies of perioperative complications by donor race, overall, and according to severity level (where higher Clavien grade indicates more severe complications). White donors were the reference group.

year of donor age was associated with a 1% relative increase in risk of respiratory and gastrointestinal complications, a 2% increase in injury and bleeding, a 3% increase in hernias, and a 4% increase in cardiac complications (Table S4). Women were significantly less likely to experience genitourinary, wound, hernia, respiratory, and gastrointestinal complications after donor nephrectomy.

Discussion

A current understanding of the perioperative risks associated with living kidney donation is vital for tailoring the informed consent process for future donor candidates and to guide development of strategies to reduce these risks (17). To improve understanding of the frequency, type, and severity of perioperative risks for donors, we integrated the national US donor registry with administrative records from a large academic hospital consortium and identified several important, novel findings: (i) The overall incidence of any perioperative complication following live donor nephrectomy was 16.8%. (ii) The most common complications were gastrointestinal (4.4%), bleeding (3.0%), respiratory (2.5%), and surgical/anesthesia-related injuries (2.4%). (iii) After adjustment for demographic and clinical factors, African American donors were 26% more likely to experience any perioperative complication and 56% more likely to experience the most severe complications, although the absolute incidence of severe complications remained low at 3.7%. (iv) Other factors associated with increased risk of any perioperative complication, and with the most severe complications, included predonation hematologic and psychiatric conditions and more recent years of donation. (v) Donation at centers with the highest annual volume of living donor nephrectomies was associated with approximately 45% lower risk of any perioperative complication and of the most severe complications.

The 16.8% overall incidence of perioperative complications after live donor nephrectomy in our study is higher than the reported incidences of 7.9% in the NIS study by Schold et al and 10.6% in the study by Patel et al but similar to the frequency of 18.4% identified by Friedman et al among 6320 US living kidney donors in 1999–2005 (8,12,14). In contrast with these prior studies, our design enabled confirmation of living donor status by linkage with the national donor registry, obviating any potential misclassification of nondonors as donors through the use of diagnostic codes alone, which may introduce inaccuracies in assessments of postdonation risk. The higher incidence of overall complications in our study compared with the work of Schold et al likely reflects differing definitions of the outcome measure. Schold et al defined perioperative complications by ICD-9 codes 996.x to 999.x (complications of surgical and medical care, not elsewhere classified); similar to the approach of Freidman et al, we broadened our definition to encompass specific complications including cardiac, respiratory, and gastrointestinal events, as well as codes related to bleeding, thrombosis, infection, and would-related complications (Table S1). We also supplemented the administrative data with information available in the OPTN and UHC records including intensive care unit stay, reoperation, and death, which likely also contributes to the higher incidence of complications in our study compared with the work by Patel et al.

After adjustment for other baseline factors, we found that African American race was independently associated with a higher risk of any perioperative complication. In the study by Friedman et al, African American race was also associated with a higher risk of perioperative complications (aOR 1.27) (14), whereas the study by Schold et al showed a trend that did not reach statistical significance (aOR 1.21) (8). African American donors have increased relative risks of mortality within 90 days postdonation (11), as well as longer-term complications after donation including new-onset hypertension and end-stage renal disease (18–20). In the nondonor population, African American race was associated with increased risk of complications after surgical procedures, such as cardiac and renal events, and even mortality in some studies (21). Notably, in our study, racial variation in perioperative risk was independent of adjustment for an array of potentially confounding baseline demographic, clinical, procedural, and center factors. Future work should attempt to determine mediators of racial variation in early risks after donor nephrectomy and examine whether perioperative complications correlate with longer-term risks among African American donors.

Table 2: Adjusted associations of baseline characteristics with risk and severity of perioperative complications in living kidney donors

Demographic trait	Any complication	Clavien grade II or higher	Clavien grade III or higher	Clavien grade IV or higher
	aOR (95% CI)			
Age at donation (per year)	1.01 (1.01–1.01)‡	1.01 (1.01–1.02)‡	1.01 (1.01–1.02)‡	1.01 (1.00–1.02)
Female	0.86 (0.78–0.94)*	0.94 (0.83–1.06)	0.96 (0.84–1.09)	0.88 (0.71–1.10)
Race				
White	Reference	Reference	Reference	Reference
African American	1.26 (1.10–1.45)*	1.39 (1.17–1.65)†	1.56 (1.30–1.88)‡	1.56 (1.15–2.11)*
Hispanic	1.01 (0.86–1.18)	1.04 (0.85–1.27)	1.20 (0.98–1.48)	1.69 (1.24–2.31)†
Other	0.94 (0.75–1.17)	0.79 (0.58–1.07)	0.83 (0.59–1.15)	0.77 (0.43–1.39)
Donor–recipient relationship				
First-degree relative	Reference	Reference	Reference	Reference
Other biological relative	0.94 (0.79–1.12)	0.89 (0.70–1.12)	0.87 (0.67–1.13)	0.83 (0.54–1.27)
Unrelated	1.00 (0.91–1.10)	1.04 (0.92–1.18)	1.04 (0.91–1.19)	0.94 (0.75–1.17)
Donor health insurance				
Insured	Reference	Reference	Reference	Reference
Uninsured	1.07 (0.93–1.24)	1.03 (0.85–1.25)	0.97 (0.79–1.20)	0.97 (0.68–1.39)
Missing	1.25 (1.10–1.41)†	1.75 (1.51–2.03)‡	1.36 (1.15–1.61)†	2.06 (1.60–2.65)‡
Body mass index, kg/m^2				
Nonobese (<30)	Reference	Reference	Reference	Reference
Obese (≥30)	1.05 (0.92–1.18)	1.20 (1.03–1.39)*	1.20 (1.02–1.41)*	1.55 (1.21–1.98)†
Missing	1.05 (0.93–1.19)	0.92 (0.78–1.08)	0.94 (0.79–1.13)	0.64 (0.45–0.92)*
Physical capacity				
No limitations	Reference	Reference	Reference	Reference
Limitations	1.12 (0.57–2.18)	0.91 (0.36–2.30)	0.69 (0.21–2.22)	1.21 (0.28–5.25)
Missing	0.83 (0.62–1.09)	0.49 (0.32–0.76)*	0.63 (0.41–0.97)*	0.10 (0.01–0.69)*
Comorbid conditions				
Hypertension	0.97 (0.84–1.11)	1.00 (0.84–1.19)	1.05 (0.87–1.26)	0.81 (0.58–1.13)
Genitourinary	1.92 (1.48–2.51)‡	2.36 (1.74–3.21)‡	2.62 (1.90–3.60)‡	1.77 (0.96–3.25)
Cardiac	0.90 (0.56–1.44)	0.98 (0.54–1.75)	0.87 (0.45–1.68)	1.25 (0.45–3.44)
Respiratory	1.12 (0.92–1.35)	1.03 (0.80–1.31)	0.92 (0.70–1.22)	1.03 (0.66–1.60)
Gastrointestinal	1.11 (0.94–1.30)	1.08 (0.88–1.32)	1.03 (0.82–1.28)	1.01 (0.70–1.47)
Hematologic	1.60 (1.18–2.18)*	1.75 (1.21–2.54)*	1.72 (1.16–2.54)*	2.78 (1.62–4.76)†
Neurologic	1.26 (0.62–2.57)	0.95 (0.37–2.43)	0.44 (0.11–1.82)	0.73 (0.10–5.33)
Endocrine	1.07 (0.93–1.23)	1.11 (0.93–1.32)	1.08 (0.90–1.31)	1.17 (0.85–1.61)
Rheumatologic	0.87 (0.36–2.14)	0.76 (0.23–2.51)	0.66 (0.16–2.77)	1.98 (0.45–8.60)
Psychiatric	1.29 (1.10–1.52)*	1.43 (1.17–1.75)†	1.52 (1.23–1.88)†	1.45 (1.01–2.08)*
Pain	1.03 (0.81–1.31)	0.92 (0.67–1.26)	0.93 (0.65–1.31)	0.89 (0.49–1.61)
Smoking	1.13 (0.97–1.31)	1.13 (0.93–1.38)	1.17 (0.95–1.45)	1.12 (0.78–1.60)
Other substance use	0.85 (0.49–1.47)	0.76 (0.36–1.59)	0.96 (0.46–2.00)	0.64 (0.15–2.65)
Procedure and center characteristics				
Nephrectomy type, intended				
Laparoscopic (nonrobotic)	Reference	Reference	Reference	Reference
Laparoscopic (robotic)	1.20 (0.90–1.59)	1.09 (0.77–1.54)	1.40 (0.99–2.00)	2.07 (1.30–3.31)*
Open	1.31 (1.06–1.64)*	0.95 (0.69–1.30)	0.85 (0.60–1.21)	1.53 (0.91–2.59)
Side of donated kidney				
Left	Reference	Reference	Reference	Reference
Right	1.02 (0.90–1.17)	0.89 (0.55–1.06)	0.87 (0.71–1.05)	0.57 (0.39–0.83)*
Payer for donation				
Commercial	0.94 (0.85–1.05)	0.78 (0.68–0.90)†	0.92 (0.80–1.07)	1.14 (0.90–1.46)
Medicare	1.05 (0.91–1.21)	1.05 (0.88–1.26)	1.18 (0.98–1.42)	1.35 (0.98–1.87)
Other	Reference	Reference	Reference	Reference
Average annual center volume				
≤10	0.85 (0.61–1.17)	0.84 (0.55–1.27)	0.78 (0.49–1.25)	0.50 (0.22–1.16)
11–50	Reference	Reference	Reference	Reference
>50	0.56 (0.51–0.61)‡	0.61 (0.54–0.69)‡	0.60 (0.53–0.68)‡	0.55 (0.44–0.68)‡
Donation year				
2008–2010	Reference	Reference	Reference	Reference
2011–2012	1.13 (1.04–1.24)*	1.27 (1.13–1.43)‡	1.30 (1.15–1.47)‡	1.69 (1.36–2.08)‡

aOR, adjusted odds ratio; CI, confidence interval.
The p-value compared with reference group: *p < 0.05–0.002, †p = 0.001–0.0001, ‡p < 0.0001.

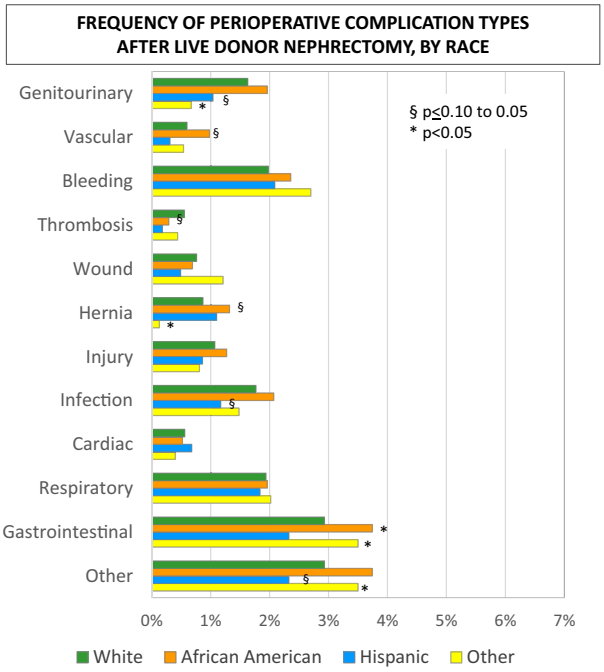

Figure 3: Frequencies of perioperative complication types by donor race. White donors were the reference group.

Our study corroborates associations of older age and obesity with increased risk of perioperative complications previously reported by Friedman et al and Patel et al (12, 14), although these factors were not significant correlates of postnephrectomy risk in other studies (8,11). Conversely, predonation hypertension was not significantly associated with increased risk of perioperative complications in our study but has been implicated in other studies (8,11). Transplant centers vary substantially in their acceptance of donors with baseline medical abnormalities, with a greater proportion of centers accepting such donors in recent years (3,4). Although long-term data on the outcomes for medically complex living kidney donors are lacking, recent data suggest that intermediate outcomes (i.e. within the first decade) for these donors and their recipients are acceptable (22–27). Further study is needed to determine whether the increased frequency of perioperative complications in the most recent years of our study (2011–2012) is robust and whether the changing clinical and demographic characteristics of accepted living kidney donors plays a role. While we adjusted for an array of baseline clinical conditions, most conditions were defined as binary (yes/no) variables, and the observed temporal trends in complications may reflect residual confounding by unmeasured baseline clinical risk.

In our study, patients who donated at centers performing the highest annual volume of donor nephrectomies (>50 cases/year) had a 44% lower relative risk of perioperative complications compared with those managed at mid-sized (11–50 cases/year) centers. Patel et al found that centers performing ≤50 cases/year had more than twice the risk of perioperative complications (aOR 2.28) as centers that performed >100 cases/year (12), suggesting further benefits with very high levels of experience. Friedman et al also reported lower complication rates (aOR 0.73) for donor nephrectomies performed at moderate-volume (≥20 cases/year) compared to lower-volume hospitals within the NIS sample (14), although in drawing data from a stratified 20% sample of inpatient admissions to acute care hospitals, representation of practice among all US transplant centers is limited. The reduction in risk associated with higher center volume may reflect benefits of the experience of clinical teams and healthcare systems that frequently participate in the surgical and perioperative care of these donors (28). Notably, in our study, small center volume (≤10 cases/year) was not associated with increased risk compared with mid-sized volume.

Our study has a number of strengths, including the verification of donor status through linkage with the national donor registry, capture of procedure-related characteristics such as nephrectomy technique (open vs. laparoscopic; robotic vs. nonrobotic), and side of nephrectomy not captured in other studies (8,12,14). Side of nephrectomy was not associated with overall complication risk, although procurement of the right kidney was associated with lower risk of the most severe complications. This likely reflects careful selection of cases for right donor nephrectomy, as the left kidney is procured in most cases of laparoscopic donor nephrectomy due to the relative technical ease and typically longer venous pedicle. A recent systematic review and meta-analysis concluded that compared with right-sided laparoscopic donor nephrectomy, left-sided nephrectomy was associated with lower risks of delayed graft function and allograft thrombosis but found no significant differences between the two approaches with respect to intraoperative or postoperative complications for the donor (e.g. estimated blood loss, conversion to open nephrectomy) or other allograft complications (e.g. graft loss, rejection) (29). While associations of robotic nephrectomy with twice the risk of Clavien grade IV or higher complications may in part reflect selection of higher risk cases (e.g. obese donors) for robotic procedures, our models were adjusted for obesity and some robotics programs use the modality routinely. This observation supports that robotic and other emerging minimally invasive (e.g. single-port) nephrectomies are not currently standard of care approaches and should be performed only by surgeons with adequate training and experience and after informed consent. Other strengths of our study include the ability to characterize an array of complication types and complication severity, while availability of present on admission diagnoses broadened description of baseline comorbidity.

Our study also has limitations. Although we were able to confirm living donor status through the OPTN donor registry, our linkage with an academic hospital consortium resulted in a donor cohort that represented approximately half of those registered in the OPTN in the period. Thus, while larger than prior studies, our results may not be generalizable to living donor nephrectomies performed at nonacademic hospitals, where procedural and center factors may differ. Notably, the baseline characteristics for the study sample were similar to that of all US living kidney donors registered in the OPTN during the same period. Due to the observational nature of our study design, we are able to describe associations but not prove causation. Our study evaluated numerous outcomes among the living kidney donor cohort and, as such, there is the possibility that some significant results were a result of random variation (Type I error).

Physical examination measurements, laboratory values, and diagnostic test results were not available to adjudicate the clinical diagnoses in our study. All sources of data used in the study are vulnerable to underascertainment, and thus we used any indication of a comorbidity or complication as an indication of that condition. While the available data capture transfusions as a key component of Clavien grade II complications, as well as procedure codes for parenteral nutrition and antibiotic infusions, we did not have access to pharmacy records and thus some grade II treatments may have been missed or misclassified as grade I events. Future linkages of cohort and administrative data should be pursued to validate the accuracy of administrative data for the identification and classification of perioperative complications. We also did not have complete data for all donors with respect to some baseline variables, such as donor health insurance and BMI. In our study, one in four living kidney donors either lacked health insurance (11.6%) or had missing information on health insurance (15.4%). Captured outcomes were limited to events during the nephrectomy hospitalization, and complications that may have presented after discharge or required readmission were not included. Given the potential risks to living kidney donors, perioperative and long-term follow-up are recommended. Living kidney donors without health insurance are more likely to be lost to follow-up and/or have missing data in follow-up reports to the national registry (30,31), possibly reflecting barriers in access to care.

In summary, linkage of the national donor registry with administrative records from an academic hospital consortium enabled characterization of perioperative complications after live donor nephrectomy in a contemporary sample, including description of complication types and severity and identification of demographic, clinical, procedural, and center-related correlates of complication risk. We found that while one in six US living kidney donors experienced a perioperative complication, the most severe complications were infrequent, affecting only 2.5% of donors. Donors who were older, men, and African Americans and those with preexisting genitourinary, hematologic, and psychiatric disorders were most likely to develop complications. Further research is needed to determine if postnephrectomy complications correlate with adverse transplant outcomes or longer-term health problems for the donor and to identify strategies to minimize the risk of perioperative complications in all donors.

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Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

References

1. OPTN (Organ Procurement and Transplantation Network)/UNOS (United Network for Organ Sharing). National Data Reports, Transplants by Donor Type. [cited 2015 Aug 1]. Available from: http://optn.transplant.hrsa.gov/converge/latestData/rptData.asp.
2. OPTN (Organ Procurement and Transplantation Network) and SRTR (Scientific Registry of Transplant Recipients). OPTN/SRTR 2011 Annual Data Report. Kidney Chapter/Living Donors. Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation. 2011 [cited 2013 Jul 24]. Available from: http://srtr.transplant.hrsa.gov/annual_reports/2011/flash/01_kidney/files/assets/downloads/publication.pdf.
3. 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: 2062–2070.
4. Taler SJ, Messersmith EE, Leichtman AB, et al. Demographic, metabolic, and blood pressure characteristics of living kidney donors spanning five decades. Am J Transplant 2013; 13: 390–398.
5. Wainright J; UNOS Research Department. Short-term living donor complications. 2013 [cited 2013 Jul 24]. Available from: unos.org.
6. Mjøen G, Oyen O, Holdaas H, Midtvedt K, Line PD. Morbidity and mortality in 1022 consecutive living donor nephrectomies:

Benefits of a living donor registry. Transplantation 2009; 88: 1273–1279.
7. Lentine KL, Patel A. Risks and outcomes of living donation. Adv Chronic Kidney Dis 2012; 19: 220–228.
8. Schold JD, Goldfarb DA, Buccini LD, et al. Comorbidity burden and perioperative complications for living kidney donors in the United States. Clin J Am Soc Nephrol 2013; 8: 1773–1782.
9. Lentine KL, Segev DL. Better understanding live donor risk through big data. Clin J Am Soc Nephrol 2013; 8: 1645–1647.
10. Davis CL, Cooper M. The state of U.S. living kidney donors. Clin J Am Soc Nephrol 2010; 5: 1873–1880.
11. Segev DL, Muzaale AD, Caffo BS, et al. Perioperative mortality and long-term survival following live kidney donation. JAMA 2010; 303: 959–966.
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. Department of Health and Human Services. Health Resources and Services Administration. 2004 Annual Report of the U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients: Transplant Data 1994-2003. [cited 2015 Aug 1]. Available from: http://www.srtr.org/annual_Reports/default.aspx
14. Friedman AL, Cheung K, Roman SA, Sosa JA. Early clinical and economic outcomes of patients undergoing living donor nephrectomy in the United States. Arch Surg 2010; 145: 356–362; discussion 62.
15. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; 240: 205–213.
16. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: Five-year experience. Ann Surg 2009; 250: 187–196.
17. Tan JC, Gordon EJ, Dew MA, et al. Living donor kidney transplantation: Facilitating education about live kidney donation-recommendations from a Consensus Conference. Clin J Am Soc Nephrol 2015; 10: 1670–1677.
18. 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.
19. Muzaale AD, Massie AB, Wang MC, et al. Risk of end-stage renal disease following live kidney donation. JAMA 2014; 311: 579–586.
20. Doshi MD, Goggins MO, Li L, Garg AX. Medical outcomes in African American live kidney donors: A matched cohort study. Am J Transplant 2013; 13: 111–118.
21. Esnaola NF, Hall BL, Hosokawa PW, et al. Race and surgical outcomes: It is not all black and white. Ann Surg 2008; 248: 647–655.
22. Young A, Storsley L, Garg AX, et al. Health outcomes for living kidney donors with isolated medical abnormalities: A systematic review. Am J Transplant 2008; 8: 1878–1890.
23. Lam NN, Lentine KL, Levey AS, Kasiske BL, Garg AX. Long-term medical risks to the living kidney donor. Nat Rev Nephrol, 2015; 11: 411–419.
24. Tent H, Sanders JS, Rook M, et al. Effects of preexistent hypertension on blood pressure and residual renal function after donor nephrectomy. Transplantation 2012; 93: 412–417.
25. Reese PP, Bloom RD, Feldman HI, et al. Mortality and cardiovascular disease among older live kidney donors. Am J Transplant 2014; 14: 1853–1861.
26. Toyoda M, Yamanaga S, Kawabata C, et al. Long-term safety of living kidney donors aged 60 and older. Transplant Proc 2014; 46: 318–320.
27. Ahmadi AR, Lafranca JA, Claessens LA, et al. Shifting paradigms in eligibility criteria for live kidney donation: A systematic review. Kidney Int 2015; 87: 31–45.
28. Ghaferi AA, Birkmeyer JD, Dimick JB. Hospital volume and failure to rescue with high-risk surgery. Med Care 2011; 49: 1076–1081.
29. Liu N, Wazir R, Wang J, Wang KJ. Maximizing the donor pool: Left versus right laparoscopic live donor nephrectomy–systematic review and meta-analysis. Int Urol Nephrol 2014; 46: 1511–1519.
30. Weng FL, Reese PP, Waterman AD, Soto AG, Demissie K, Mulgaonkar S. Health care follow-up by live kidney donors more than three yr post-nephrectomy. Clin Transplant 2012; 26: E300–E306.
31. Schold JD, Buccini LD, Rodrigue JR, et al. Critical factors associated with missing follow-up data for living kidney donors in the United States. Am J Transplant 2015; 15: 2394–2403.

Supporting Information

Additional Supporting Information may be found in the online version of this article.

Table S1: Databases and coding definitions for baseline characteristics and outcome variables.

Table S2: Baseline characteristics of the study sample of living kidney donors compared with all living kidney donors recorded in the OPTN during the study period (2008–2012).

Table S3: Adjusted associations of sociodemographic characteristics with baseline comorbidity in living kidney donors.

Table S4: Adjusted associations of baseline characteristics with perioperative complication types in living kidney donors.