Minimizing Morbidity of Organ Donation: Analysis of Factors for Perioperative Complications After Living-Donor Nephrectomy in the United States

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Background. Expansion of living kidney donation through liberalizing acceptance criteria invites a renewed focus on safety and outcomes. Wide variability exists in reported donor complications, and associated risk factors are ill defined. Use of administrative data can overcome the bias of single-center studies and identify variables associated with untoward events.

Methods. The study population consisted of 3074 living kidney donors from 28 centers during 2004 and 2005. Data from a large healthcare registry were used to retrospectively identify the study cohort. Perioperative complications were identified using ICD-9-CM coding and classified according to the Clavien system. Logistic regression models were constructed to identify donor and center factors associated with complications.

Results. There were no perioperative deaths. The overall complication rate was 10.6% and major complications defined by Clavien grade ≥3 was 4.2%. The prevalence of tobacco use, obesity, and hypertension, was 7.8%, 2.4%, and 2.3%, respectively. Age >50 (odds ratio [OR]=1.81, 95% confidence interval [95% CI]=1.25–2.61), tobacco use (OR=1.41, 95% CI=1.02–1.94), obesity (OR=1.92, 95% CI=1.06–3.46), and annual center volume ≤50 (OR=2.28, 95% CI=1.68–3.09), were significantly associated with overall morbidity, however only annual center volume ≤50 (OR=2.07, 95% CI=1.27–3.37) was significantly associated with a risk of major complications.

Conclusions. The inclusion of donors with tobacco abuse, obesity, and age >50 increases complications; however, the risk of major morbidity is small. Use of administrative data represents an important tool to facilitate the reconciliation of an increased need for organ donors with the concern for donor safety.

Keywords: Kidney, Donor, Transplant, Complications.

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Kidney transplantation has become the optimal treatment for end-stage renal disease, with an expected increase in survival compared with hemo- or peritoneal dialysis therapy (*1*). The greatest barrier to timely renal transplantation continues to be organ availability, and nearly 70 000 patients in the United States are currently listed for a deceased donor organ (*2*). Despite efforts to increase the number of deceased donors, the demand for renal transplantation continues to outpace organ availability (*3*). Living donor kidney transplantation (LDKT) has been increasingly used during the last decade to help decrease both the number of patients and shorten the time spent on the wait list. The percentage of kidney transplants from live donors has steadily been increasing and, since 2001, live donors comprise more than 50% of all donors.

The growth in living kidney donors can be attributed to a number of factors: the widespread recognition that LDKT is superior to deceased donor kidney transplantation (DDKT) in that it affords earlier transplantation and improved long-term survival (*4*), the advent of laparoscopic donor nephrectomy which has improved the time and physical difficulty of donor recovery (*5–8*), and the liberalization of donor acceptance criteria to increase the pool of potential donors (*9*). The consideration of individuals previously excluded from donation appears to be gaining wider acceptance. This phenomenon, coupled with the increasing prevalence of obesity and hypertension among the general population (*4*), make it likely that donors once excluded for these conditions may be an increasing source of living donor kidneys in the coming years. This changing paradigm of live donor utilization necessarily invites a renewed focus on donor safety and outcomes.

Reports of donor complications in the literature demonstrate wide variability and the risk factors associated with donor nephrectomy are ill defined. Current understanding is primarily based upon single institution experiences that lack standardized systems of classifying complications (*4*, *7*, *10*, *11*). The need for a standardized classification system has previously been articulated by several groups (*12*, *13*), and is echoed here to emphasize that it is paramount to both the selection and consent processes of the potential organ donor.

METHODS

Data Source/Study Population

In this retrospective cohort study, we identified living kidney donors by using discharge coding data from a large

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healthcare registry, the University HealthSystem Consortium (UHC) Clinical Database. It is a collection of patient-level discharge data, including administrative and clinical data used to provide benchmarking measures (*14*). The UHC Clinical Database has previously been used to examine outcomes of various surgical procedures including laparoscopic versus open appendectomy, hernia repair, and bariatric surgery (*15–17*).

For this study, discharge data from 2004 and 2005 for patients admitted with a primary diagnosis of kidney donor, as identified by the ICD-9-CM code V59.4, were extracted from the UHC database. Of these, only the subset of patients with a primary procedure diagnosis of nephroureterectomy (ICD-9-CM code 55.51), or primary procedure diagnosis of laparoscopy (ICD-9-CM code 54.21) and secondary procedure diagnosis of nephroureterectomy were included. This eliminated discharge data for preoperative workup admissions and the admissions during which no procedure was performed; this yielded 3,074 patients from 28 centers. Comorbidities and complications were identified with the use of ICD-9-CM coding data. Complications were stratified using a modified Clavien system: Grade 1, requiring no pharmacologic treatment, or only antiemetic, antipyretic, analgesic, diuretic agent; Grade 2, requiring pharmacologic treatment with an agent other than those allowed for in grade 1, requiring non-autologous, postoperative blood transfusion; Grade 3, requiring surgical, endoscopic, or interventional radiologic procedure; Grade 4, life-threatening complication; Grade 5, death (*18*, *19*).

Two different mechanisms were used to further validate the data beyond the internal review process used by the administrators of the database. First, the discharge data was compared to OPTN (*2*) data with respect to number of cases per year for each center; 27 of the 28 centers were within 5 cases for each year of data, one center had data within 15 cases for one year. Additionally, the discharges captured from our institution were compared with our own internal database with respect to number of discharges per year, patient demographics (age, gender, and race) ICD-9-CM diagnosis and procedure codes, and length of stay. There was 100% congruence between the data.

Statistical Analysis

Chi-square analysis was used to test bivariate relationships between donor/center risk factors and perioperative complications and to determine subsequent entry into multivariate logistic regression models, the requirement for which was a $P<0.10$. Adjusted odds ratios were calculated using logistic regression; separate equations were formulated for all complications and major complications. Means were compared using analysis of variance (ANOVA); a Bonferroni correction was applied to multiple comparisons to maintain a familywise alpha of 0.05. Results for the chi-square test and ANOVA were reported using p-values, and odds ratios were reported with 95% confidence intervals (95% CI). All data management and statistical analysis was performed using SPSS version 14 (SPSS Inc., Chicago, IL).

RESULTS

Donor demographics data are shown in Table 1; mean age was 40±11 years. Mean annual center volume was 82±43. As expected, the donor population, irrespective of age, was generally healthy. Table 1 also provides information on the prevalence of identified comorbidities, with 18.9% of donors having one comorbidity, and 4.1% having 2 or more.

TABLE 1. Donor characteristics

Characteristic	N[a]	Percent
Age, yrs		
≤30	666	21.67
31–50	918	29.86
41–50	955	31.07
>50	535	17.40
Gender		
F	1801	58.59
M	1273	41.41
Race		
White	1977	64.31
African American	516	16.79
Asian	80	2.60
Native American	13	0.42
Other	131	4.26
Unknown	357	11.61
Comorbidity		
Tobacco use	240	7.80
Hyperlipidemia	108	3.51
Asthma	98	3.19
Hypertension	72	2.34
Obesity	75	2.43
Sleep apnea	19	0.62
Alcohol abuse	5	0.16
Coronary artery disease	3	0.10
Atrial fibrillation	2	0.06
Previous myocardial infarct	1	0.03
Status after cardiac pacemaker	1	0.03
Congestive heart failure	1	0.03

[a] Total N=3074.

There was no perioperative mortality. The overall complication rate was 10.6% and major complication rate, defined by Clavien grade 3 or greater, was 4.2%. Center volume was categorized to ≤50, 51–100, and >100. Complication rates by center volume were as follows: 14.1% for ≤50, 12.9% for 51–100, and 6.4% for >100 ($P<0.001$). Similarly, the major complication rates were 5.0% for ≤50, 5.8% for 51–100, and 2.3% for >100 ($P<0.001$).

Grade 1 and 2 complications versus grade 3 and greter complications were chosen to differentiate major versus minor as it was felt that need for an invasive intervention should classify a complication as being major due to the additional risk introduced by the intervention. Major and minor complications, with associated rates of occurrence, are listed in Table 2.

Therapeutic procedures performed postkidney donation are listed in Table 3; 72 donors (2.3%) had a subsequent procedure. Four donors underwent re-exploration, three for bleeding (postoperative day range 0 to 2), and one for an

intra-abdominal abscess (postoperative day 3). Two donors required hemodialysis during their initial admission.

Several covariates were tested for an association with perioperative complications. These included age, gender, race, tobacco use, hypertension, obesity, respiratory disease, and annual center volume. Age >50 (odds ratio [OR]=1.81, 95% confidence interval [95% CI]=1.25–2.61), tobacco use (OR=1.41, 95% CI=1.02–1.94), obesity (OR=1.92, 95% CI=1.06–3.46), and annual center volume ≤50 (OR=2.28, 95% CI=1.68–3.09), were significantly associated with overall postoperative morbidity (Table 4). Only annual center volume ≤50 was significantly associated with serious complications (Clavien grade 3 or greater; OR=2.07, 95% CI=1.27–3.37).

The UHC dataset tracks readmissions to the original hospital. There were 44 (1.4%) readmissions out of 3074 donors. The various indications for readmission are provided in Table 5. Of the six wound infections, three were treated with excisional debridement; the three intra-abdominal collections were treated with percutaneous drainage. Excluding incisional hernia, the mean number of days from discharge to readmission was 8.7±10.5; the mean for incisional hernia repair was 266±91 days from discharge. Three donors were readmitted for a second time, all for nausea and vomiting, and all within 1 day of the first readmission.

TABLE 2. Postoperative complications by Clavien grade

Grade/complication	N[a]	Rate (%)
1		
Atelectasis	48	1.56
Ileus	51	1.66
Fever	20	0.65
Pleural effusion	6	0.20
2		
Need for blood transfusion	26	0.85
UTI	13	0.42
Cellulitis	12	0.39
Wound infection	12	0.39
Pneumonia	7	0.23
3		
Intraoperative injury	32	1.0
Vessel	9	0.29
Pleura	9	0.29
Spleen	6	0.20
Bowel	4	0.13
Diaphragm	3	0.10
Bladder	1	0.03
Pneumothorax	5	0.16
Urine leak	1	0.03
4		
Acute renal failure	9	0.29
Rhabdomyolysis	3	0.10
Pulmonary embolus	2	0.07
Congestive heart failure	2	0.07
Myocardial infarction	1	0.03

[a] Total N=3074.
UTI, urinary tract infection; CHF, congestive heart failure; MI, myocardial infarction.

TABLE 3. Therapeutic procedures

Procedure	N[a]	Percent
Respiratory		
Repair of pleura	9	0.29
Insertion of chest tube	5	0.16
Prolonged ventilation (<96 h)	2	0.07
Reintubation	1	0.03
Laryngo-tracheoscopy	2	0.07
Cardiovascular		
PTCA	1	0.06
Right heart cardiac cath	1	0.03
IABP	1	0.03
IVC filter	1	0.03
Renal		
Hemodialysis	2	0.07
Return to operating room		
Reopening of recent laparotomy site	4	0.13
Bleeding	3	0.10
Intraabdominal abscess	1	0.03
Other		
Percutaneous abdominal drainage	2	0.07

[a] Total N=3074.
PTCA, percutaneous transluminal coronary angioplasty; IABP, intraaortic balloon pump; IVC, inferior vena cava.

DISCUSSION

The altruistic act of donating a kidney is a personal decision; however, it is the responsibility of the medical community to ensure that the donor is informed of the risks of the procedure and the potential short and long-term complications. The current state of knowledge regarding donor complications is challenged by the design of previous studies, with most data derived from single centers with short-term

TABLE 4. Adjusted odds ratios for all complications

Risk factors	AOR	95% CI Lower	95% CI Upper	*P* value
Age				
≤30	1.00		Reference	
31–40	1.13	0.79	1.59	0.442
41–50	1.14	0.8	1.61	0.367
>50	1.81	1.25	2.61	**0.001**
Obesity	1.92	1.06	3.45	**0.037**
Tobacco use	1.41	1.02	1.94	**0.027**
Center volume				
>100	1.00		Reference	
51–100	2.15	1.59	2.91	**<0.001**
≤ 50	2.28	1.68	2.08	**<0.001**

Values in bold indicate statistical significance.
AOR, adjusted odds ratio; 95% CI, 95% confidence interval.

TABLE 5. Indications for readmission

Indication	N[a]	Percent	Time from discharge[b]
Ileus/Constipation/emesis	20	0.65	3
Incisional hernia	7	0.23	267
Wound infection	6	0.20	10
Intraabdominal collection	3	0.10	22
Deep venous thrombosis	2	0.07	8
Pneumonia	2	0.07	7.5
Pleural effusion	1	0.03	2
Cholecystitis	1	0.03	27
Pain	1	0.03	5
Hematoma	1	0.03	10

[a] Total N=3074.
[b] Number of days from initial discharge, value is mean if N>1.

follow-up (*5*, *20–22*). Most studies with long-term data have been criticized for missing patients who have been lost to follow-up (*23*, *24*). It is within this vacuum that there have been recent calls by the lay and medical community for greater outcomes information and oversight among living organ donors (*25*, *26*). Designing such studies has been hampered by a lack of funding, although a recent initiative by the NIH may address some of these issues (*27*). Defining the nature of the complications, their potential morbidity, and risk factors for complications will allow a transplant center working with a potential donor to make an informed decision with regards to donation.

It is clear from this work, as well as others, that live donor nephrectomy is performed with a relatively low risk for perioperative morbidity. This study adds to our current understanding of perioperative complications by defining for the first time variables that are associated with complications. The identification of risk factors for poor outcomes is the first step towards minimizing morbidity. Once identified, postoperative care in the higher-risk subset may potentially be focused on prevention.

As might be expected, smoking, obesity, greater age, and lower center volume are associated with complications. These covariates have been well-described among non-donors undergoing surgery (*28–30*). Fortunately major complications were rare; most of these were technical in nature. Only lower center volume was associated with the risk of major complications.

From the perspective of patient selection, obesity, smoking, and age >50 were all found to be associated with increased risk for complications, although most of these were relatively minor. These findings, in our opinion, hardly warrant the exclusion of donors with these identifiable risk factors, especially since the overall risk is quite minimal. However, in this day and age of ever-increasing demands on medical practitioners to wholly explain the potential risks of medical interventions, these findings may help bolster the process of informed consent.

One issue that this study was unable to address accurately is the difference in outcomes between laparoscopic and open donor nephrectomy. Currently, there in no ICD-9-CM code for laparoscopic nephrectomy. It is unclear whether laparoscopic nephrectomy is associated with an increased risk of donor complications. In a systematic review of 44 studies by Tooher et al. (*6*), no difference in donor perioperative morbidity was detected when comparing laparoscopic to open nephrectomy. Additionally, in a multicenter study, Davis et al. found similar rates of perioperative morbidity between the different laparoscopic and open procedures (*4*). From an administrative data standpoint a more accurate assessment can be made once laparoscopic nephrectomy has a unique ICD-9-CM code.

Another limitation to this study is the inability to detect complications that may occur beyond the perioperative period. Not all administrative databases capture readmission data and for those that do, donor readmissions may not occur at the original hospital, as donors may seek healthcare at other institutions. The UHC database is able to identify those donors who were readmitted to the original donor hospital only. Although it is intuitive that donors may seek further medical care from the same institution, especially large university-based hospitals, this may not be true. Thus, those that can be identified may represent a small fraction of readmissions. Capturing long-term donor complications may only be possible by diligent follow-up by individual centers or through funded multicenter studies. Mandates by UNOS that centers must follow their donors for two years may improve the current understanding; however, they are unlikely to address long-term concerns regarding renal function. In the current era, where there is a high degree of media and legislative scrutiny of living donor practices, there is a natural disincentive to report donor results and complications. Administrative data divests itself from this bias as the data is collected by trained coders who function independently of physicians, patient care, and studies utilizing the data.

Our work highlights the ability of administrative data to help overcome the inherent bias of single-center studies, and their value as an efficient means of examining large numbers of patients. Administrative data have previously been used to examine a variety of medical issues to help identify risk factors for poor outcomes (*30–35*). The inherent statistical power is obvious, but their use has been cautioned because of the reliance on hospital coding data. It is this type of data, however, that lend themselves toward the analysis of donor and center risk factors for particular outcomes such as morbidity and mortality. The addition of a validated and standardized tool to assess surgical complications facilitates such an analysis and can abrogate some of the limitations of single center analyses.

In the context of organ donation, use of administrative data, along with a standardized tool to measure complications, represents an important methodology to facilitate the reconciliation of an increased need for organ donors with the concern for donor safety. As the various criteria for acceptable donors continue to be liberalized, concomitant with an increasing prevalence of obesity in society, there may be a foreseeable increase in the rate of complications. The issue of donor safety will continually need to be revisited to maintain an accurate, real-time assessment of the practice of living kidney donation, especially so that the potential donor is able to make the most informed decision possible.

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