The effect of gender on nephrectomy perioperative outcomes: a national survey

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Introduction: *The effect of gender on complications after surgery is controversial. We examine the effect of gender on five short term nephrectomy outcomes.*

Materials and methods: *Within the Health Care Utilization Project, Nationwide Inpatient Sample (NIS) we focused on nephrectomies performed within the most contemporary years (1998-2007). We tested the rates of blood transfusions, extended length of stay, in-hospital mortality, as well as intraoperative and postoperative complications, stratified according to gender. Multivariable logistic regression analyses fitted with general estimation equations for clustering among hospitals further adjusted for confounding factors. Separate multivariable analyses were performed for open radical nephrectomy (ORN), open partial nephrectomy (OPN), laparoscopic radical nephrectomy (LRN) and laparoscopic partial nephrectomy (LPN).*

Results: *Overall, 48172 nephrectomies were identified. Of those, female patients accounted 39.4% of cases (n = 18966). Female gender was associated with higher rates of blood transfusions ($p < 0.001$) and higher rates of prolonged length of stay ($p < 0.001$). Conversely, female gender was associated with lower rates of postoperative complications ($p < 0.001$) and in-hospital mortality ($p = 0.015$). In multivariable analyses, female patients had higher rates of blood transfusion (OR = 1.22, $p < 0.001$) but significantly lower rates of postoperative complications (OR = 0.81, $p < 0.001$) and in-hospital mortality. No statistically significant differences were recorded for intraoperative complications and length of stay beyond the median (all $p > 0.05$). Gender as a predictor of outcomes was most pronounced in OPN and LPN.*

Conclusions: *Nephrectomies performed in female patients are associated with lower rates of postoperative complications and in-hospital mortality. Conversely, blood transfusions rates are higher in these patients. Gender disparities in perioperative outcomes are most pronounced after OPN.*

Key Words: morbidity, kidney cancer, nephrectomy, gender

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Introduction

Despite recent advances in the medical management for renal cell carcinoma (RCC), surgical resection is the only curative treatment and represents the standard of care for suspected renal malignancy. The past two decades have seen the advent of nephron-sparing surgery, which has become the recommend treatment of small renal masses when technically feasible.[1] To date, numerous studies have demonstrated lower rates of complications following nephrectomy at tertiary referral

centers.[2,3] However, only a single study has examined complication rates in a population-based sample.[4]

While the impact of gender on surgical outcomes has been widely debated across many surgical disciplines,[5-15] and the impact of gender on radical cystectomy has been reported,[16-19] the association between gender and surgical outcomes of nephrectomy remains poorly understood. In the present study, we assess the effect of gender on nephrectomy morbidity and mortality. Within a large contemporary (1998-2007) population-based cohort of individuals undergoing nephrectomy, we performed a risk-adjusted assessment of the rates of blood transfusions, intraoperative and postoperative complications, prolonged length of stay beyond the median of 5 days, as well as in-hospital mortality. Insight into the effect of gender on major urologic oncology procedures is critical in reducing disparities in care and improving patient outcomes.

Materials and methods

Data source

Data from the most contemporary years (1998-2007) of the Nationwide Inpatient Sample (NIS) were abstracted. The NIS includes inpatient discharge data collected via federal-state partnerships, as part of the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project. As of the year 2007, the NIS contained administrative data on 8,043,415 discharges from 1044 hospitals within 40 states, approximating 20% of community hospitals within the United States, including public hospitals and academic medical centers. The NIS is the sole hospital database in the United States with charge information on all patients regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured.

Sample population and surgical procedures

Patients with a primary diagnosis of cancer of the kidney were identified using the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic code: 189.0. Secondary diagnostic codes (ICD-9-CM 197.0, 197.7, 198.x) were used to identify patients with metastases, and were excluded from any further analysis. Relying on the ICD-9 procedure codes, patients who underwent PN (55.4) were abstracted. Laparoscopic surgical approach was identified via concurrent procedures code for laparoscopic exploration (54.21).

Baseline patient and hospital characteristics

Patient characteristics include age at surgery (in years), coded as a continuous variable. Those less than 18 years of age were not considered. Gender and race (white, black, Hispanic, other races including Asian, Pacific Islander, Native American, or other unspecified, and unknown) were also examined. Baseline Charlson Comorbidity Index (CCI) was calculated according to Charlson et al,[20] and adapted according to Deyo and colleagues.[21] Hospital characteristics include the hospital region (Northeast, Midwest, South, West), which was obtained from the American Hospital Association Annual Survey of Hospitals, and defined by the United States Census Bureau.[22] Hospital caseload was defined according to the number of nephrectomies performed annually. Subsequently, hospital caseload was categorized into three equal tertiles: low (1-5 nephrectomies per year), intermediate (6-15 nephrectomies per year), and high (≥ 16 nephrectomies per year). The hospital's academic status was obtained from the AHA Annual Survey of Hospitals. A hospital is considered to be a teaching hospital if it has an American Medical Association (AMA)-approved residency program, is a member of the Council of Teaching Hospitals or has a ratio of full-time equivalent interns and residents to beds of 0.25 or higher.

Intraoperative, postoperative complications, and blood transfusions during hospitalization

The NIS records up to 15 diagnoses and procedures per in-hospital stay. The presence of any complication was defined using ICD-9 diagnoses 2 through 15. Additionally, 11 groups of postoperative complications were identified, namely: complications occurring in the digestive system, respiratory complications, hemorrhage or hematoma, cardiac-related complications, postoperative infections, vascular complications, seroma complicating a procedure, operative wound related complications and other. For statistical analysis purposes, we stratified patients by 0 versus 1 or greater complications during hospitalization. We used the same stratification for homologous blood transfusion rate analysis.

Length of stay, and in-hospital mortality

Length of stay, provided by the NIS, is calculated by subtracting the admission date from the discharge date. Length of stay was dichotomized according to the median (1-5 versus ≥ 5 days). In-hospital mortality information is coded from disposition of patient. Patients with missing or invalid length of stay or in-hospital mortality status were not considered within the current study (n = 33).

Statistical analysis

Descriptive statistics focused on frequencies and proportions for categorical variables. Means, medians and ranges were reported for continuously coded

variables. Chi-square and independent-sample t tests were used to compare the statistical significance of differences in proportions and means, respectively.

We first compared univariable rates of blood transfusion, intraoperative complications, postoperative complications, length of stay beyond the median and in-hospital mortality, stratified by gender. In addition to the overall postoperative complication rate, separate analyses targeted subtypes of postoperative complications: cardiac, respiratory, digestive, hemorrhage or hematoma, vascular, wound, seroma, postoperative infections and miscellaneous complications.

We subsequently constructed multivariable logistic regression models to quantify the effect of gender on all nephrectomy outcomes of interest while controlling for factors known to be confounding. The models controlled for age, race, baseline Charlson comorbidity index, hospital region and caseload, year of surgery, academic status, insurance status and surgical technique. All models relied on generalized estimating equations (GEE-models) to further adjust for clustering among hospitals.[23] To better understand the effect of gender on the different approaches to nephrectomy, multivariable models were constructed for the five main outcomes within each of the four surgical techniques assessed: open radical nephrectomy (ORN), laparoscopic radical nephrectomy (LRN), open partial nephrectomy (OPN) and laparoscopic partial nephrectomy (LPN).

All tests were two-sided with a statistical significance set a $p < 0.05$. Analyses were conducted using the R statistical package (the R foundation for Statistical Computing, version 2.12).

Results

Between 1998 and 2007, 48172 nephrectomies were recorded within the NIS. Of these, 91.7% (44186) were performed by an open approach, 8.3% (3986) were performed laparoscopically. Baseline characteristics of patients undergoing nephrectomy in the NIS between 1998 and 2007 are listed in Table 1. Within our cohort, the majority of patients (60.6%) were male versus 39.4% female. In comparison to male patients, female patients were older (mean age 62.7 versus 61.8, $p < 0.001$), had more comorbidity (CCI ≥ 3: 6.9% versus 5.7%, $p < 0.001$), were less likely to be treated at high AHC institutions (31.2% versus 32.4%, $p < 0.001$) or academic institutions (56.1% versus 56.5%, $p = 0.030$) and were less likely to receive a partial nephrectomy (16.8% versus 18.2%, $p < 0.001$).

When compared to male patients, female patients had higher rates of blood transfusions (11.5% versus 9.2%, $p < 0.001$), as well as higher rates of prolonged length of stay (32.9% versus 30.7%, $p < 0.001$), Table 2. Conversely, female patients had lower rates of postoperative complications (14.6% versus 17.1%, $p < 0.001$). Specifically, the rates of digestive, hemorrhage, cardiac and postoperative infection complications were lower in female patients, compared to male patients. Additionally, females experienced a significantly lower rate of in hospital mortality (0.6% versus 0.8%, $p = 0.015$).

In multivariable analysis adjusted for clustering and controlling for age, race, CCI, hospital region and caseload, year of surgery, academic status, insurance status and surgical technique (ORN, LRN, OPN and LPN), Table 3, female patients were at higher risk of transfusion (OR = 1.22, $p < 0.001$), but were less likely to experience postoperative complications (OR = 0.81, $p < 0.001$), and in-hospital mortality (OR = 0.66, $p < 0.001$) when compared to male patients. After stratification according to surgical approach, the same findings were reported for ORN and OPN, Table 4. Conversely, LRN outcomes only differed in the likelihood of receiving a blood transfusion (OR = 1.45, $p = 0.023$), while LPN outcomes differed for blood transfusions (OR = 3.19, $p = 0.047$) and postoperative complications (OR = 0.42, $p = 0.021$).

Discussion

Nephrectomy represents one of the main management options for enhancing renal masses, with partial nephrectomy being the gold standard for renal masses amenable to the technique.[1] Nonetheless, morbidity after kidney surgery is reported to be approximately 20% in single institution series from centers of excellence.[1-3] To date, a single population-based study has provided insight into the complication rate following nephrectomy in a representative population-based sample.[4] Joudi et al focused on differences in the complication rates between partial and radical nephrectomy, as well as the effect of complications on in-hospital mortality and hospital charges. In the current manuscript, we examine the impact of gender on risk stratification, to aid surgeons in the appropriate management and counseling of their patients.

Our analyses showed higher rates of blood transfusion (11.5% versus 9.2%, $p < 0.001$) in female patients, compared to male patients. Conversely, overall complication rates were lower (14.6% versus 17.1%, $p < 0.001$) in female patients. Since important population differences may account for the observed differences, we performed a multivariable adjustment for the key patient and institutional characteristics, namely age, race, baseline CCI, hospital region and caseload, year of surgery,

TABLE 1. **Descriptive characteristics of 48172 patients treated with radical or partial nephrectomy, stratified according to gender, Nationwide Inpatient Sample, 1998-2007**

Variables	Overall	Male	Female	p value
No. of patients	48172	29206 (60.6)	18966 (39.4)	—
Age, yr				**< 0.001**[†]
Mean (median)	62.2 (70)	61.8 (62)	62.7 (64)	
Range	40-95	18-97	18-104	
Race				**< 0.001**
White	28351 (58.9)	17398 (59.6)	10953 (57.8)	
Black	3287 (6.8)	1873 (6.4)	1414 (7.5)	
Other	16534 (34.3)	9935 (34.0)	6599 (34.8)	
CCI[†]				**< 0.001**
0	30169 (62.6)	18443 (63.1)	11726 (61.8)	
1	12426 (25.8)	7467 (25.6)	4959 (26.1)	
2	2609 (5.4)	1630 (5.6)	979 (5.2)	
≥ 3	2968 (6.2)	1666 (5.7)	1302 (6.9)	
Hospital region				**0.003**
Northeast	9568 (19.9)	5850 (20.0)	3718 (19.6)	
Midwest	10641 (22.1)	6315 (21.6)	4326 (22.8)	
South	19032 (39.5)	11516 (39.4)	7516 (39.6)	
West	8931 (18.5)	5525 (18.9)	3406 (18.0)	
Year				**0.303**
1998	1547 (3.2)	926 (3.2)	621 (3.3)	
1999	3916 (8.1)	2392 (8.2)	1524 (8.0)	
2000	4362 (9.1)	2632 (9.0)	1730 (9.1)	
2001	4411 (9.2)	2699 (9.2)	1712 (9.0)	
2002	5208 (10.8)	3138 (10.7)	2070 (10.8)	
2003	5258 (10.9)	3194 (10.9)	2064 (10.9)	
2004	5466 (11.3)	3278 (11.2)	2188 (11.5)	
2005	5595 (11.6)	3337 (11.4)	2258 (11.9)	
2006	6112 (12.7)	3701 (12.7)	2411 (12.7)	
2007	6297 (13.1)	3909 (13.4)	2388 (12.6)	
Annual hospital caseload				**< 0.001**
1-5	17209 (35.7)	10199 (34.9)	7010 (37.0)	
6-15	15591 (32.4)	9558 (32.7)	6033 (31.8)	
≥ 16	15372 (31.9)	9449 (32.4)	5923 (31.2)	
Academic status				**0.030**
Non-teaching	21131 (43.9)	12696 (43.5)	8435 (44.5)	
Teaching	27041 (56.1)	16510 (56.5)	10531 (55.5)	
Insurance status				**< 0.001**
Private	22319 (46.3)	14290 (48.9)	8029 (42.3)	
Federally-funded	23476 (48.7)	13459 (46.1)	10017 (52.8)	
Other	2377 (4.9)	1457 (5.0)	920 (4.9)	
Surgical approach				**0.644**
Open	44186 (91.7)	26803 (91.8)	17383 (91.7)	
Laparoscopic	3986 (8.3)	2403 (8.2)	1583 (8.3)	
Radical versus partial				**< 0.001**
Radical	39659 (82.3)	23878 (81.8)	15781 (83.2)	
Partial	8513 (17.7)	5328 (18.2)	3185 (16.8)	

[†]independent sample t test; CCI = Charlson comorbidity index.

TABLE 2. **Intraoperative and postoperative outcomes after nephrectomy stratified according to gender**

	Overall	Male	Female	OR (CI 95%)	p value
No. of patients	48172	29206 (60.6)	18966 (39.4)	-	-
Blood transfusion	4856 (10.1)	2678 (9.2)	2178 (11.5)	1.29 (1.21-1.36)	**< 0.001**
Intraoperative complication	1625 (3.4)	965 (3.3)	660 (3.5)	1.06 (0.95-1.17)	**0.296**
Postoperative complication					
Overall	7756 (16.1)	4984 (17.1)	2772 (14.6)	0.83 (0.79-0.88)	**< 0.001**
Respiratory	2108 (4.4)	1318 (4.5)	790 (4.2)	0.92 (0.84-1.01)	**0.07**
Digestive	2791 (5.8)	1891 (6.5)	900 (4.7)	0.72 (0.66-0.78)	**< 0.001**
Hemorrhage or hematoma	2700 (5.6)	1690 (5.8)	1010 (5.3)	0.92 (.85-0.99)	**0.032**
Cardiac	818 (1.7)	533 (1.8)	285 (1.5)	0.82 (0.71-0.95)	**0.007**
Vascular	86 (0.2)	51 (0.2)	35 (0.2)	1.06 (0.69-1.63)	**0.80**
Seroma	42 (0.1)	24 (0.1)	18 (0.1)	1.16 (0.63-2.13)	**0.64**
Operative wound	39 (0.1)	29 (0.1)	10 (0.1)	0.53 (0.26-1.09)	**0.08**
Postoperative infections	339 (0.7)	244 (0.8)	95 (0.5)	0.60 (0.47-0.76)	**< 0.001**
Other	38 (0.1)	16 (0.1)	22 (0.1)	2.12 (1.11-4.04)	**0.019**
Length of stay, days					
Length of stay > 5 days	15193 (31.5)	8961 (30.7)	6232 (32.9)	1.11(1.06-1.15)	**< 0.001**
In-hospital mortality	340 (0.7)	228 (0.8)	112 (0.6)	0.76 (0.6-0.95)	**0.015**

TABLE 3. **Multivariable logistic regression analysis predicting the rate of intraoperative and postoperative outcomes following nephrectomy, by gender**

Outcomes	Female versus male odds ratio (95% CI)*	p value
Blood transfusion	1.22 (1.15-1.30)	**< 0.001**
Intraoperative complication	1.04 (0.94-1.15)	**0.49**
Postoperative complication		
Overall	0.81 (0.77-0.85)	**< 0.001**
Respiratory	0.90 (0.82-0.99)	**0.029**
Digestive	0.70 (0.65-76)	**< 0.001**
Hemorrhage or hematoma	0.89 (0.83-0.97)	**0.007**
Cardiac	0.77 (0.66-0.89)	**< 0.001**
Operative wound	0.47 (0.23-0.98)	**0.043**
Postoperative infections	0.59 (0.46-0.75)	**< 0.001**
Vascular	1.05 (0.68-1.61)	**0.84**
Seroma	1.07 (0.58-1.97)	**0.84**
Other	2.04 (1.07-3.9)	**0.031**
Length of stay > 5 days	1.02 (0.98-1.06)	**0.39**
In-hospital mortality	0.66 (0.52-0.82)	**< 0.001**

*model adjusted for age, race, baseline Charlson comorbidity index, hospital region, hospital caseload, year of surgery, academic status, insurance status and surgical technique (open radical nephrectomy, laparoscopic radical nephrectomy, open partial nephrectomy and laparoscopic partial nephrectomy.

TABLE 4. **Multivariable logistic regression analysis predicting the rate of intraoperative and postoperative outcomes during hospitalization stratified by surgical technique. All odds ratios (OR) utilize the male probability as the referent value**

Outcomes	Open radical Nx		Open partial Nx		Lap radical Nx		Lap partial Nx	
	OR (95% CI)*	p value	OR (95% CI)*	p value	OR (95% CI)*	p value	OR (95% CI)*	p value
Blood transfusion	1.19 (1.11-1.27)	< 0.001	1.36 (1.16-1.58)	< 0.001	1.45 (1.05-2.01)	0.023	3.19 (1.02-10)	0.047
Intraoperative complication	1.00 (0.89-1.12)	0.99	1.26 (0.97-1.64)	0.09	1.24 (0.76-2.01)	0.39	**	**
Postoperative complication***	0.81 (0.77-0.86)	< 0.001	0.78 (0.68-0.88)	< 0.001	0.86 (0.69-1.06)	0.15	0.42 (0.20-0.88)	0.021
Length of stay > 5 days	1.01 (0.97-1.06)	0.55	1.09 (0.98-1.21)	0.11	0.89 (0.73-1.09)	0.26	0.68 (0.36-1.26)	0.22
In-hospital mortality	0.70 (0.55-0.89)	0.004	0.33 (0.13-0.88)	0.026	0.51 (0.16-1.63)	0.26	**	**

*model adjusted for age, race, baseline Charlson comorbidity index, hospital region, hospital caseload, year of surgery, academic status and insurance status.
**too few incidents to draw conclusions.
***rate of any postoperative complication.

academic status, insurance status. Surgical technique (ORN, LRN, OPN and LPN) was also controlled for. Multivariable analyses of these confounders, with adjustment for clustering, corroborated the initial findings.

After stratification according to surgical technique, our results showed that the protective effect of female gender on postoperative outcomes persisted after ORN, OPN and LPN. Conversely, gender failed to reach independent predictor status after LRN. These observations indicate that, on average, female nephrectomy complications are lower than those recorded for men, except for blood transfusions. When specific subtypes of complications are examined, it is interesting that female patients were less likely to experience wound and digestive complications. Although these findings are slightly unexpected, other investigators have reported decreased rates of wound disruption and anastomotic leakage in female patients undergoing abdominal surgery.[24-26] Finally, our analyses demonstrated that female gender is associated with a decreased risk of mortality after ORN and OPN. Numerous hypotheses may be proposed to explain the recorded observations, though the relation between gender and the observed outcomes remains unexplained.

The importance of gender in various medical and surgical conditions has previously been addressed. Carbonell et al noted a protective effect of female gender on multivariable analysis assessing the risk of complication associated with laparoscopic cholecystectomy (OR = 0.74).[27] This finding was replicated by Murphy et al in a population-based study of 1.1 million patient discharges.[10] Similar findings have been shown in bariatric surgery,[5,13] lung resection,[8] and esophageal variceal bleeding.[11] Conversely, an adverse effect of female gender has been described after coronary artery bypass graft, as elucidated by Vaccarino et al.[15,28]

Gender differences in outcomes have also been reported in urologic literature. In a population-based analysis of the NIS from 1998 to 2002 by Konety et al, gender failed to reach independent predictor status in multivariable analyses adjusted for comorbidity status and year of surgery. In contrast, female patients were at lower risk of primary complications, defined as those directly attributable to the cystectomy.[16] However, the authors did not adjust for hospital teaching status and diversion type, which may affect the outcome rates. Cardenas-Turanzas et al also examined the effect of gender on RCC outcomes. In a population-based analysis of the Texas Hospital In-Patient Discharge Data Collection (n = 1493), the authors showed that females are at risk of increased blood products utilization and length of hospital stay after RCC. Their analyses were limited to the state of Texas and the selection of examined

complications did not allow direct comparison with other large database. Finally, Siegrist et al also reported higher rates of transfusions and higher blood loss in females within a large institutional cohort of 1142 patients.[18]

Limitations of the current study include the selection bias related to the database: only 20% of the United States population is represented in the National Inpatient Sample. Other explanations may also be advanced to ascertain for the differences, consisting of patient variables (tumor stage, grade and size, obesity, medication) and socioeconomical determinants. It is possible that women are more likely to present with favorable tumor characteristics, which could explain their better perioperative outcomes. Although this was previously reported in a single-institution study,[29] the limitations of the dataset could not allow us to verify this hypothesis within the NIS. Unavailability of individual surgical volume represents another limitation. Ideally, our analyses should also have been controlled for this important variable. Additionally, administrative records may underestimate the rate of complications. For example, a 17% underestimation was previously reported relative to blood bank records.[30] Our mortality estimates are based on in-hospital rates. It is possible that the true mortality is therefore underestimated. Moreover, administrative data do not allow standardized collection of complications, such as the criteria defined by Martin and subsequently modified by Donat.[31-34] Specifically, claims data do not allow us to grade the severity of complications according to the Clavien classification.[35] Although this represents an important weakness of our study, this limitation was shared by all other population-based reports.

Conclusions

Nephrectomies performed in female patients are associated with lower rates of postoperative complication and in-hospital mortality. Conversely, blood transfusions rates are higher in these patients. Gender disparities in perioperative outcomes are most pronounced after OPN. □

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