Does gender influence morbidity or mortality in the surgical treatment of renal masses?

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Abstract

Introduction: We determine the relationship between gender and surgical morbidity after radical nephrectomy (RN) and partial nephrectomy (PN) for renal masses on a population level.
Methods: We conducted a population-based, retrospective study using the Canadian Institute for Health Information Discharge Abstract Database. This included 20 286 RNs (82.5%) and 4292 PNs (17.5%) from April 1, 1998 to March 31, 2008. Complications were identified by ICD-9 and 10 codes, and comorbidity was assessed with the Charlson Index. The association between gender and in-hospital complication rates and mortality were examined using the Chi-square test, as well as with multivariable logistic regression, adjusting for explanatory variables including type of surgery, age, and comorbidity.
Results: Overall, men experienced a higher unadjusted complication rate than women (35.1% vs. 32.7%), as well as a higher unadjusted in-hospital mortality rate (1.46% vs. 0.84%), respectively. Men also demonstrated significantly higher rates of cardiac, wound, nephrectomy-specific, and medical complications. Women experienced fewer complications than men after RN (*p* = 0.0002), but not after PN (*p* = 0.33). On multivariable logistic regression analysis, women had a lower overall complication rate (odds ratio [OR] 0.94, 95% confidence interval [CI] 0.88-0.99), and a lower in-hospital mortality rate (OR 0.64, 95% CI 0.49-0.83) after kidney surgery.
Conclusions: In our population-based analysis, in-hospital morbidity after renal surgery was significantly lower for women. Further study is needed to determine if the observed effect is related to differences in surgical difficulty, perioperative care, or unmeasured confounders.

Introduction

Studies investigating gender-related morbidity and mortality of renal surgery for renal cell carcinoma (RCC) are not commonly seen in the urologic literature. New healthcare programs are striving to decrease treatment-related disparities, as well as to monitor use and access to care. There has been an increase in the detection of small renal masses due to the increased use of abdominal imaging. Radical nephrectomy (RN) and partial nephrectomy (PN) are the standard of care for a renal mass which is suspected to be malignant.[1-3] An understanding of the gender-related morbidity of distinct treatment interventions can be important in counselling patients and offering prognostic information.[2-5] Large epidemiological studies using databases in Europe and the United States, including the Pathological Anatomical National Automated Archive (PALGA) and National Cancer Database, respectively, have investigated gender differences in the presentation of RCC.[4,5]

Current published data of surgical morbidity tend to originate from academic tertiary referral centers,[6,7] which may not accurately reflect the morbidity of renal surgery in community practices. Although increased age has already been shown to be associated with increased morbidity and mortality after renal surgery,[8] the impact of other patient characteristics on postoperative complications are not clearly defined. Women tend to present with smaller tumours, lower grade, and lower stage disease. Also, women may have less severe comorbidities (i.e., hypertension, diabetes, chronic obstructive pulmonary disease, congestive heart failure) that may allow them to experience better recovery after surgery.[8]

Reporting surgical complication data is important in that it allows physicians to more accurately counsel their patients prior to intervention. Our objective was to determine the effect of gender on patient morbidity and in-hospital mortality after RN and PN.

Methods

Patient selection

We performed a population-based, retrospective, observational study using the Canadian Institute for Health

Information (CIHI) Discharge Abstract Database (DAD), which provides information from 9 out of 10 Canadian provinces.[9] Data for this study included all hospitalized patient records treated by either RN or PN. These records were identified using either specific Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP) codes which correspond to the 9th revision of the International Classification of Disease (ICD-9), or Canadian Classification of Health Interventions (CCI) procedure codes, which correspond to the ICD-10.

The study included discharge abstracts on all patients treated by either RN or PN at acute inpatient facilities from April 1, 1998 to March 31, 2008.[9] We excluded patients under 18 years old and patients who underwent nephrectomy for anything other than a solid or cystic renal mass (e.g., urothelial carcinoma, infection, polycystic kidney disease, non-functional kidney). This dataset is a re-analysis of a previously published dataset assessing the morbidity of kidney surgery.[8] Research Ethics Board approval was obtained from the University of Toronto.

Comorbidities

We used the Deyo adaptation of the Charlson Index as a measure of comorbidity. This method has been validated for use with administrative data using ICD-9 and ICD-10 diagnosis codes.[10,11]

Complications

In-hospital complications were identified using ICD-9 and ICD-10 diagnostic and procedure codes that have been described in other published studies of renal cell carcinoma.[6,7] Complications were grouped into major organ systems: cardiac, pulmonary, vascular, wound/bleeding, genitourinary, nephrectomy-specific, miscellaneous surgical, and miscellaneous medical. Nephrectomy-specific complications included control kidney bleeding, drainage of kidney, need for dialysis, repair of ureter, ureteral stenting, and RN after index PN.[8]

Statistical analyses

Descriptive information on pertinent variables was generated for all patients, as well as stratified by treatment type (RN vs. PN). Mean, ranges, and standard deviations were reported for continuous variables and proportions were reported for categorical variables. The mean of continuous variables were compared using the t-test, whereas categorical variables were compared using the chi-square test, univariate and multivariable logistic regressions. Since the model was meant to determine associations rather than being used as a prediction tool, a reductionist model-building strategy was not used to determine variable inclusion; rather, all predetermined variables were included in the model (i.e., gender, year of surgery, patient age, geographical region, surgeon and hospital volume, Charlson score, procedure type [RN or PN], and patient income). Odds ratio (OR) estimates and 95% confidence intervals (CI) were obtained for all strata. Logistic model calibration and discrimination were assessed with the Hosmer-Lemeshow and c-statistic, respectively. Statistical significance was defined as a p value less than 0.05. All analyses were performed using SAS v.9.2 (SAS Institute Inc, Cary, NC).

Results

A total of 24 578 kidney surgeries were included in our study: 20 286 (82.5%) RN and 4292 (17.5%) PN from April 1, 1998 to March 31, 2008 (Table 1). Overall, more men were treated than women: 14 769 (60.1%) vs. 9810 (39.9%), respectively. In our population, men had significantly higher comorbidity than women, with a greater proportion of men with Charlson scores of 2 (7.6% vs. 5.7%) and ≥3 (3.6% vs. 2.2%) compared with women ($p < 0.0001$) (Table 1). The specific comorbidities which were greater for men and statistically significant included myocardial infarction, peripheral vascular disease, peptic ulcer disease, complications of diabetes mellitus, renal insufficiency, all cancers (excluding kidney cancer), severe liver disease, and human immunodeficiency virus. However, the proportion of dementia patients was similar ($p = 0.0748$) and connective tissue disorder ($p < 0.0001$) was the only comorbidity that was greater for women (Table 1).

The unadjusted overall complication rate for all kidney surgery was higher in men compared with women, 35.1% vs. 32.7% ($p < 0.0001$). Even after adjusting for potential confounders on multivariable logistic regression analysis, women had a lower overall complication rate (OR 0.94, 95% CI 0.88-0.99). When complications were stratified by major organ system, our results demonstrated that men had a higher rate of cardiac, wound, nephrectomy-specific, and medical miscellaneous complications; however male gender was associated with lower genitourinary and miscellaneous surgical complication rates.

There was no significant difference ($p = 0.37$) in the proportion of RNs (82.7% vs. 82.3%) or PNs (17.3% vs. 17.7%) performed in men versus women, respectively (Table 1). Women experienced fewer complications after RN compared to men ($p = 0.0002$), but there was no difference after PN ($p = 0.33$). Even after adjusting for covariates, women had fewer complications after RN (OR 0.92, 95% CI 0.87-0.98, $p = 0.011$); however, gender had no effect on complications after PN (OR 0.99, 95% CI 0.87-1.14, $p = 0.93$) (Table 2).

Although complications increased with age for both men and women, the absolute difference between patients aged

Table 1. Nephrectomy patient demographics

Variable	Total (%)	Male (%)	Female (%)	p value
Nephrectomy type				0.3733
Total	24 579	14 769 (60.1)	9810 (39.9)	
Radical nephrectomy	20 286 (82.5)	12 215 (82.7)	8071 (82.3)	
Partial nephrectomy	4292 (17.5)	2553 (17.3)	1739 (17.7)	
Age				0.0001
<50 years	4613 (18.8)	2636 (17.9)	1977 (20.1)	
50-59 years	5885 (23.9)	3613 (24.5)	2272 (23.2)	
60-69 years	6609 (26.9)	4179 (28.3)	2430 (24.8)	
70-79 years	5852 (23.8)	3463 (23.4)	2389 (24.3)	
>80 years	1620 (6.6)	878 (5.9)	742 (7.6)	
Mean age (standard deviation)	61.4 (13.0)	61.49 (12.5)	61.34 (13.6)	0.3879
Charlson score				<0.0001
0	18 521 (75.4)	10871 (73.6)	7650 (78.0)	
1	3635 (14.8)	2255 (15.3)	1380 (14.1)	
2	1681 (6.8)	1118 (7.6)	563 (5.7)	
≥3	742 (3.0)	525 (3.5)	217 (2.2)	
Comorbidities				
Myocardial infarction	717 (2.92)	537 (3.64)	180 (1.83)	<0.0001
Congestive heart failure	529 (2.15)	322 (2.18)	207 (2.11)	0.7642
Peripheral vascular disease	300 (1.22)	233 (1.58)	167 (0.68)	<0.0001
Cerebrovascular disease	207 (0.84)	128 (0.88)	79 (0.80)	0.1842
Dementia	38 (0.15)	16 (0.11)	22 (0.22)	0.0748
Pulmonary disease	1265 (5.15)	776 (5.25)	489 (4.98)	0.3526
Connective Tissue disorder	111 (0.45)	44 (0.3)	67 (0.68)	<0.0001
Peptic ulcer disease	87 (0.35)	69 (0.47)	18 (0.18)	0.0012
Liver disease	46 (0.19)	31 (0.21)	15 (0.15)	0.4775
Diabetes mellitus	2377 (9.67)	1464 (9.91)	903 (9.20)	0.1630
Complications of diabetes mellitus	286 (1.16)	196 (1.33)	90 (0.92)	0.0222
Paraplegia	47 (0.19)	31 (0.21)	16 (0.16)	0.5570
Renal insufficiency	807 (3.28)	570 (3.86)	237 (2.41)	<0.0001
All localized cancer (excluding kidney)	849 (3.45)	572 (3.87)	277 (2.83)	<0.0001
All metastatic cancer (excluding kidney)	31 (0.13)	21 (0.14)	10 (0.10)	0.4304
Severe liver disease	1816 (7.69)	1194 (8.09)	622 (6.35)	<0.0001
Human immunodeficiency virus	9 (0.0003)	9 (0.06)	0 (0.0)	0.0145

<50 and those ≥80 was greater for men than for women (18.5% vs 14.4%, $p < 0.0001$) (Fig. 1a). When compared by gender, the difference observed between overall complications became more pronounced with increasing age category, with men always having higher complication rates than women (≤50: 1.43%, age 50-59: 2.06%, age 60-69: 1.08%, age 70-79: 4.63%, age ≥80: 5.54%; $p < 0.0001$). On the other hand, the increase in the complication rate with higher comorbidity was not significantly different between men and women (Fig. 1a).

The unadjusted in-hospital mortality rate was almost double (1.46% vs. 0.84%) in men compared with women ($p < 0.0001$). Using a multivariable logistic regression analysis for in-hospital mortality, adjusting for potential confounders, we found that women had a reduced risk of in-hospital death (OR 0.64, 95% CI 0.49-0.83) (Table 3).

Women were less likely to experience in-hospital mortality after kidney surgery when compared to men for all age groups ($p < 0.0001$) (Fig. 1b). Similarly, female gender had a lower in-hospital mortality for each Charlson score category ($p = 0.0012$). When mortality was examined by gender and stratified by treatment type, we found that women had a lower in-hospital mortality compared to men for both RN and PN (0.97% vs. 1.62%; 0.23% vs. 0.67%, respectively, $p < 0.0001$) (Fig. 1b).

Discussion

New healthcare programs and government mandated quality initiatives aim to decrease treatment-related disparities. Institutions are attempting to monitor patient's access to care and treatment decision-making. Yet, studies examining renal

Table 2. Multivariable logistic regression analyses assessing predictors of complications after radical and partial nephrectomy

Variable	Radical nephrectomy		Partial nephrectomy	
	OR (95% CI)	p value	OR (95% CI)	p value
Age category		<0.0001		<0.0001
<50	Referent		Referent	
50-59	0.98 (0.88-1.08)		1.11 (0.92-1.35)	
60-59	1.14 (1.03-1.25)		1.27 (1.05-1.53)	
70-79	1.39 (1.26-1.53)		1.62 (1.32-1.98)	
≥80	1.74 (1.52-1.98)		2.36 (1.59-3.50)	
Charlson category		<0.0001		<0.0001
0	Referent		Referent	
1	1.88 (1.73-2.05)		1.66 (1.38-1.99)	
2	3.57 (3.19-4.00)		2.45-1.86-3.24)	
≥3	6.22 (5.18-7.48)		5.68 (3.72-8.66)	
Gender (F vs. M)	0.92 (0.87-0.98)	0.011	0.99 (0.87-1.14)	0.93

OR: odds ratio; CI: confidence interval; F: female; M: male.

surgery stratified by gender are not frequently reported in the urologic literature. While reports have had varied results on gender equality in the type of surgery performed, our study showed that men and women were equally likely to undergo RN or PN. Also, we found that men had an absolute difference of 2.4% more complications than woman. Women had a lower overall complication rate even after adjusting for potential confounders as noted above (i.e., gender, year of surgery, patient age, geographical region).

Our analysis revealed that in-hospital mortality for both RN and PN was lower for women. A recent publication using Nationwide Inpatient Sample data (1998-2007) reported that women were less likely to experience postoperative complications and in-hospital mortality.[12] After stratification by surgical technique, Sammon and colleagues found that female gender was associated with a lower incidence of complications from open RN, open and laparoscopic PN, but not for laparoscopic RN. [12]

When we analyzed gender effect by age, complications were higher in men compared to women for all age
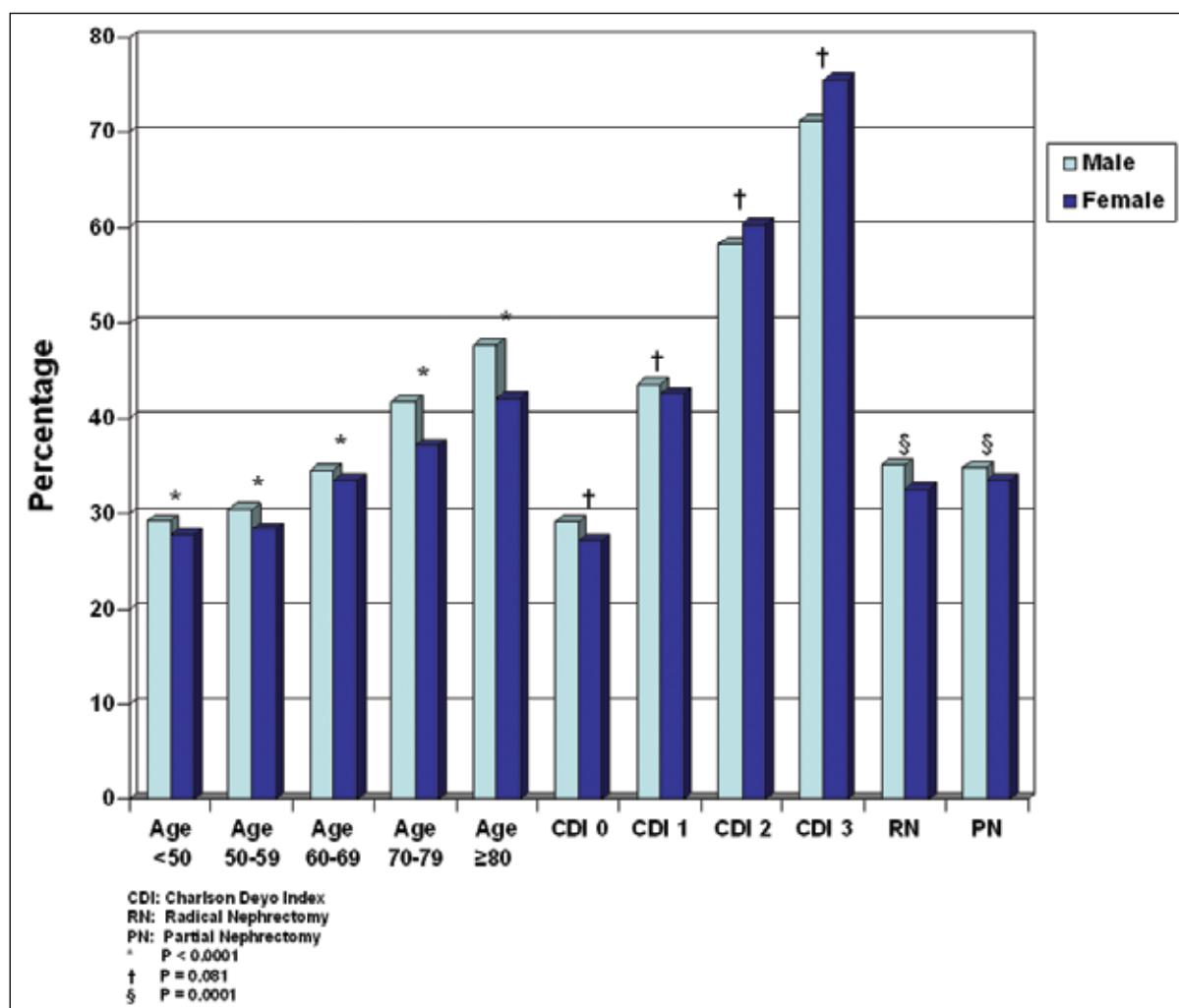
Fig. 1a. The effect of explanatory variables on all-complications stratified by gender.

categories and the observed gender difference was more pronounced in older age groups (Fig. 1a). A recent multicentre international study showed an age/gender benefit for younger woman (<59 years).[13] Rampersaud and colleagues consider this is related to hormonal changes,[13] although it is likely multifactorial. Multiple reports have demonstrated increasing age to be associated with a higher complication rate, including in-hospital mortality, after other genitourinary surgeries (i.e., radical prostatectomy).[14] Interestingly, the multicentre international study with 5654 patients found that age was an independent prognostic factor of disease-specific survival for women, but not for men. The risk of RCC-specific death increases by about 1% with each year increase in age.[13] In addition to increased postoperative complications, we observed that men were at a greater risk of in-hospital mortality for each age category (Fig. 1b).

Our study failed to demonstrate a gender disparity in the use of PN to treat renal masses, which is in contrast to other studies. Dulabon and colleagues showed that men have a 1.22 times greater odds of being treated with PN compared to women.[15]

This is despite data from the Surveillance, Epidemiology and End-Results (SEER) program suggesting that men present with larger, higher grade and higher stage tumours than women, which may require some men to receive RN.[16] Utilizing PN helps prevent potential chronic kidney disease (CKD), which is important given the increasing diagnoses of small renal tumours.[17,18] Advanced age has already been demonstrated as an independent risk factor for CKD; to help prevent future renal deterioration, there is increasing emphasis on using kidney preservation surgery for appropriate renal masses.[3,15] If a gender disparity exists in the use of PN in the United States, the reasons for this need to be studied further.

Validation studies assessing the use of ICD-9 and ICD-10 diagnosis codes from administrative data in the identification of comorbidity and complications have demonstrated good agreement with patient medical records.[11] A number of studies have examined the CIHI diagnostic and procedural data using chart review as the gold standard and found high agreement for primary diagnosis (81%-95%) and secondary diagnosis (88%-99%).[9,10] In-hospital mortality was over 99% accurate.
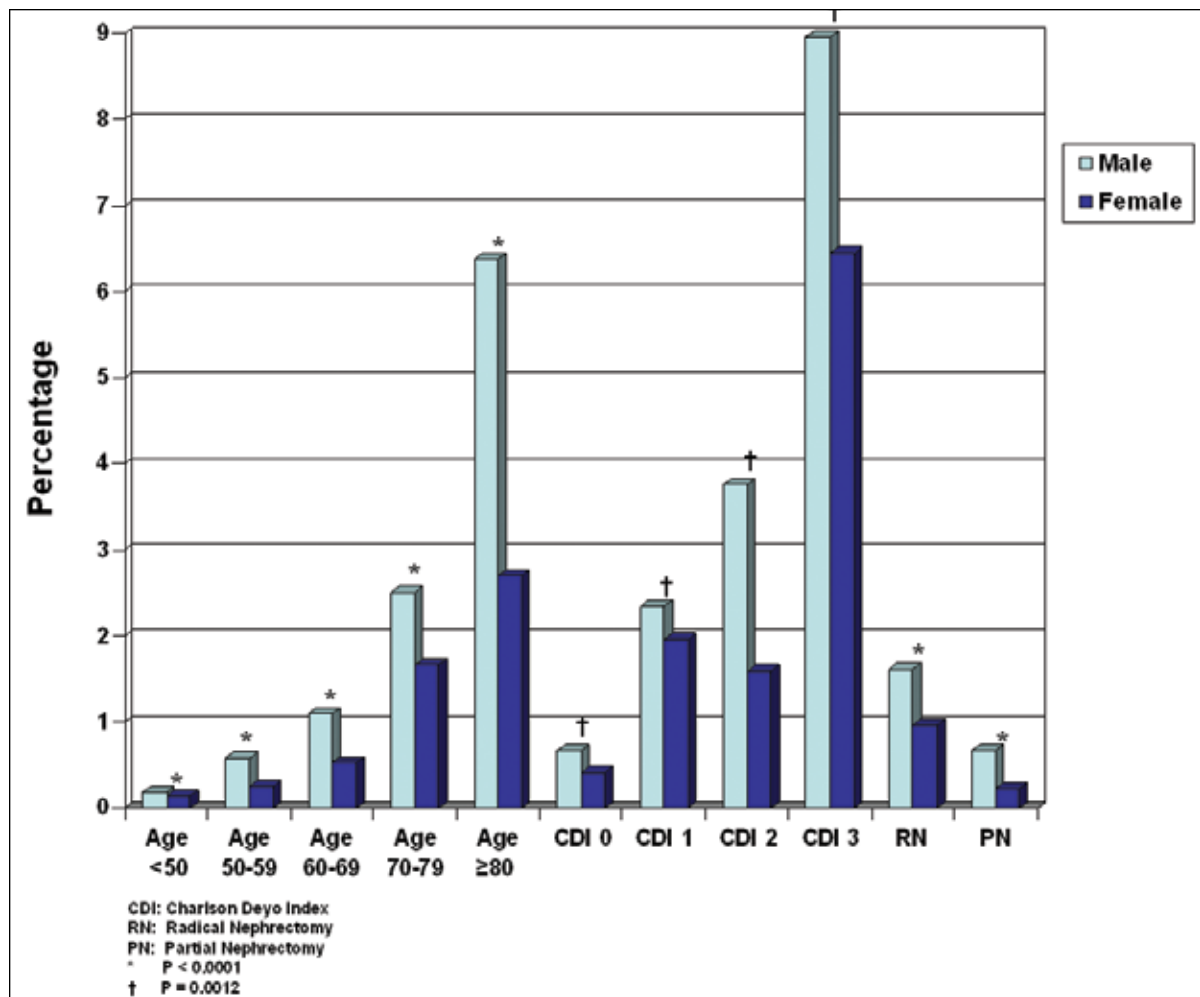

Fig. 1b. The effect of explanatory variables on in-hospital mortality stratified by gender.

Table 3. Multivariable logistic regression analysis assessing factors associated with in-hospital mortality

Variable	OR	95% CI	p value
Gender (F vs. M)	0.64	0.49-0.83	0.0009
Age <50	Referent	Referent	
50-59	2.39	1.08-5.29	<0.0001
60-69	4.00	1.90-8.41	<0.0001
70-79	8.59	4.14-17.7	<0.0001
≥80	18.1	8.61-37.9	<0.0001
Charlson category			
0	Referent	Referent	
1	4.50	3.32-6.10	<0.0001
2	4.88	3.51-6.77	<0.0001
≥3	13.9	9.45-20.4	<0.0001
Procedure (PN vs. RN)	0.45	0.29-0.71	0.0006

OR: odds ratio; CI: confidence interval; F: female; M: male; PN: partial nephrectomy; RN: radical nephrectomy.

One of the main limitations of our study is its retrospective nature, which makes the data susceptible to the effects of unmeasured confounders. Factors that could have affected the postoperative complications, such as a patient's body mass index, tumour size, stage, hospital setting and performance status, were not recorded in this database. It is well-known that tumour size and stage, which we could not account for, are important factors in the treatment selection for RCC. A multi-institutional, international study by Chen and colleagues demonstrated that female patients had lower grade renal tumours when compared to male.[19] However, they did not observe a statistically significance difference in mean tumour size between men and women. Also, we did not have length of stay, readmission rate, and Clavien grade for the complications, which would have provided a more comprehensive assessment of perioperative morbidity.

Estimates of comorbidities and complications using administrative datasets can be criticized since they can be undercoded. Re-abstraction studies demonstrate sensitivity of 53% to 99% for major medical conditions,[9] thus some comorbidity information is invariably lost. However, given that the degree of undercoding is unlikely to differ between men and women, this should not explain the gender difference in the observed complications of kidney surgery. In addition, the capture of in-hospital mortality is nearly 100%. Thus, we feel that our study provides a good estimate of the gender effect on in-hospital morbidity and mortality.

Conclusions

Our population-based analysis, which includes data from both community and tertiary-care hospitals, demonstrated a lower complication and in-hospital mortality rate after renal surgery for women compared to men. The difference in complication rates appears to be restricted to patients undergoing RN and is more pronounced in the elderly. Further study is needed to determine if the observed effect is related to differences in surgical difficulty or if it is related to confounders, such as tumour size and tumour stage.

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