



## Effect of the Need for Preoperative Dialysis on Perioperative Outcomes on Patients Undergoing Laparoscopic Nephrectomy: An Analysis of the National Surgical Quality Improvement Program Database

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<b>OBJECTIVE</b>	To investigate whether patients requiring dialysis are a higher risk surgical population and would experience more perioperative adverse events even when undergoing a perceived less invasive operation as a laparoscopic radical nephrectomy (LRN). LRN is generally a well-tolerated surgical procedure with minimal morbidity and mortality. Prior to transplantation, dialysis patients will often have to undergo a LRN to remove a native kidney with a suspicious mass.
<b>MATERIALS AND METHODS</b>	Patients in the American College of Surgeons National Surgical Quality Improvement Program who underwent a LRN between 2011 and 2016 were included. Patients were stratified by the need for preoperative dialysis 2 weeks prior to surgery, and perioperative outcomes were compared. A multivariable logistic regression analysis was performed to test the association between the need for preoperative dialysis and perioperative risk.
<b>RESULTS</b>	There were 8315 patients included in this analysis of which 445 (5.4%) patients required preoperative dialysis. Patients who required preoperative dialysis had more minor ( $P < .0001$ ) and major ( $P = .0025$ ) complications, a higher rate of return to the operating room ( $P = .002$ ), and a longer length of stay ( $P < .0001$ ) than those patients not requiring preoperative dialysis. In a multivariate analysis, the need for preoperative dialysis was independently associated with adverse perioperative outcomes (OR = 1.45, CI = 1.08-1.95, $P = .015$ ).
<b>CONCLUSION</b>	Patients requiring preoperative dialysis were more likely to experience a perioperative complication and have a longer length of stay. For LRNs performed prior to transplantation, further risk stratification is needed, and treatment sequencing may need to be reconsidered. UROLOGY 124: 154–159, 2019. © 2018 Elsevier Inc.

Surgery is the cornerstone of treatment for localized renal tumors suspected to be renal cell carcinoma (RCC).<sup>1</sup> Whether radical or partial nephrectomy, excision of localized renal masses results in very high cure rates with low patient morbidity and mortality.<sup>2</sup> End-stage renal disease is a risk factor for the development of renal cancer in patients' native kidneys, however studies have shown that these tumors, often acquired cystic kidney cancer,<sup>3</sup> have an indolent course.<sup>4-5</sup> Often, patients undergoing a renal transplantation evaluation will be

found to have tumors in their native kidneys,<sup>6</sup> and the clinical challenge will arise as to whether these tumors should be removed prior to, at the time of, or after transplantation. Some transplant centers will require that the native kidney with a tumor be removed prior to transplantation to establish a histologic diagnosis in order to risk stratify the patient's cancer, if present.

Chronic kidney disease has been shown to have significant negative health consequences in many settings.<sup>7-10</sup> Perioperatively, chronic kidney disease, and/or end-stage renal disease has been correlated with adverse surgical outcomes.<sup>11,12</sup> Furthermore, the negative health correlation between increasing age and end-stage renal disease is quite dramatic.<sup>13</sup> Although minimally-invasive surgery is often considered to be almost "risk-free," there is evidence demonstrating that laparoscopic procedures can carry a

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significant risk for complications in vulnerable populations, such as patients with end-stage renal disease.<sup>14,15</sup> Thus, there may exist a false sense of security in performing laparoscopic radical nephrectomies in patients with localized renal masses who have end-stage renal disease requiring renal replacement therapy.

In this study, we sought to evaluate the effect of the need for preoperative dialysis on patients undergoing laparoscopic radical nephrectomy (LRN). We hypothesized that although a relatively well-tolerated and low complication surgery, the need for preoperative dialysis would have a significant impact on perioperative outcomes and hospital length of stay (LOS) on patients undergoing a LRN.

## METHODS

Data for this study were obtained from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP). The NSQIP database collects information from patients postsurgery from participating institutions. Postoperative complications, preoperative health data, and demographic information are collected to allow for complete analysis and outcome assessment. For this study, patients between the years 2011-2016 were identified by the Current Procedural Terminology code for laparoscopic nephrectomy (50545). Demographic information, health status, and outcomes information for these patients were collected. Study patients were stratified by the need for preoperative dialysis, a variable captured in NSQIP as the status of renal function at least 2 weeks prior to surgery. Due to the uncertainty whether their renal failure was due to surgical complications or unresolved previous health concerns, patients who reported renal failure requiring dialysis within 30 days postoperatively were excluded from the study. After exclusions for missing data, the total study population that was analyzed was 8315.

For patients undergoing a laparoscopic nephrectomy during the study period, information was collected on patient demographics, comorbidities, American Society of Anesthesiologists (ASA) score, smoking history, functional status, and body mass index (BMI). The age of patients was then divided into different age categories (<40, 40-49, 50-59, ≥60) as well as BMI (<18.5 = underweight, 18.5-25 = normal weight, 25-30 = overweight, and obese = >30). Estimated glomerular filtration rate (GFR) was also calculated and recorded for nondialysis patients. Patient demographic data were then evaluated for significance against status of preoperative dialysis using the chi-square test of association or Fischer's exact test.

The outcomes of interest for this study were reported complications that occurred within 30 days or less after surgery, length of postsurgical hospital stay, and return to the operating room within 30 days of surgery. Each complication was grouped uniformly into a grade of severity based on the Clavien-Dindo classification as either minor (I-II), major (III-IV), or death (V). American College of Surgeons NSQIP reported complications include: superficial incisional skin infection, pneumonia, pulmonary embolus, urinary tract infection, transfusion, deep vein thrombosis, deep incisional skin infection, wound infection, reintubation, failure to wean off ventilator more than 48 hours postoperation, cardiovascular accident, cardiac arrest, myocardial infarction, sepsis, and death. Fischer's exact test was used to determine statistical significance of each complication against dialysis status. To further assess for univariate differences in

complication rates among patients stratified by dialysis status and grouped into severity levels, the Cochran-Armitage test for trends was applied.

After adjusting for comorbidity burden, a multivariate ordinal regression analysis was performed to test for association between preoperative dialysis status and complication severity, hospital LOS, and return to operating room within 30 days. A *P* value of less than .05 was considered statistically significant. All statistical analysis was performed using SAS version 9.4 software.

## RESULTS

Eight thousand three hundred fifteen patients were included in this analysis. Of the total cohort, 61.2% of the patients were male, and 85.9% were Caucasian. Stratified by the preoperative variable of needing dialysis 2 weeks prior to surgery, there were 445 (5.4%) patients who required preoperative dialysis while the remaining 7870 (94.6%) patients did not.

Significant differences existed between the 2 populations. (Table 1). Patients who were dialysis-dependent were more likely to be male (*P* <.0001), younger than 60 years of age (*P* <.0001), and non-Caucasian (*P* <.0001). Also, dialysis patients had higher preoperative rates of diabetes, hypertension, and congestive heart failure (CHF) (all *P* <.0001), expected comorbidities which are causative of and often coexist with end-stage renal disease. The dialysis-dependent group also had a higher rate of ASA scores above 3 (*P* <.0001) compared to the nondialysis group. There was no statistically significant difference in the rates of smoking, functional status, or chronic obstructive pulmonary disease (COPD) between groups. Median baseline estimated glomerular filtration rate (eGFR) for patients not on dialysis was 77.5 mL/min (interquartile range (IQR) = 62.1-92.8 mL/min).

Tables 2 and 3 collate the type and frequency, stratified by Clavien grade, of postoperative complications between the 2 groups. In the dialysis group, 17.5% of patients had a minor complication, and 7.6% of patients had a major complication. Five (1.1%) patients in this group died within 30 days of surgery. In the nondialysis group, 9.9% and 3.0% of patients had a minor and major complication, respectively. Thirty-five (0.4%) patients in this group died within the 30 days of surgery. The most common minor and major complications in the 2 groups were the need for a blood transfusion (12.1% in preoperative dialysis group vs 5.8% in no preoperative dialysis group) and unplanned reintubation (2.0% in the preoperative dialysis group and 0.74% in the no preoperative dialysis group) (both complications had *P* values <.05). Patients who required preoperative dialysis had more minor (*P* <.0001) and major (*P* = .0025) complications than those patients not requiring preoperative dialysis. The death rate between the 2 groups approached statistical significance (*P* = .06), that is, patients requiring preoperative dialysis had a statistically higher likelihood of dying postoperatively when compared to those not requiring preoperative dialysis.

Finally, 17 (3.8%) patients in the preoperative dialysis group had an unplanned return to the operating room within 30 days after surgery compared to 131 (1.7%) patients in the nondialysis group (*P* = .002). The median and mean LOS in patients requiring preoperative dialysis were 3 and 4.2 days (range = 0-44 days); and, the median and mean LOS in patients not requiring preoperative dialysis were 3 and 3.3 days (range = 0-73 days), respectively. The mean LOS was significantly longer in patients requiring preoperative dialysis (*P* <.0001). Also, patients who required preoperative dialysis were more likely to have a LOS

**Table 1.** Preoperative descriptive characteristics of study population

	Dialysis		P Value
	Yes (n = 445) n (%)	No (n = 7870) n (%)	
Sex			
Male	312 (70.1)	4776 (60.7)	<.0001
Female	133 (29.9)	3094 (39.3)	
*Age			
<40	27 (6.1)	411 (5.3)	<.0001
40-49	64 (14.4)	784 (10.0)	
50-59	134 (30.1)	1845 (23.6)	
≥60	220 (49.4)	4787 (61.2)	
*Race			
Caucasian	202 (48.8)	5924 (88.2)	<.0001
African American	186 (44.9)	588 (8.8)	
Asian	19 (4.6)	162 (2.4)	
Other	7 (1.7)	42 (1.7)	
*ASA scores			
≤3	253 (57)	7474 (95)	<.0001
4	191 (43)	383 (4.9)	
5	0	1 (<0.1)	
Median estimated GFR	N/A	**77.5 mL/min (IQR = 62.1-92.8)	
Diabetes	141 (31.7)	1637 (20.8)	<.0001
COPD	24 (5.4)	440 (5.6)	1.00
CHF	14 (3.1)	56 (0.7)	<.0001
Hypertension	378 (84.9)	5045 (64.1)	<.0001
Smoking	73 (16.4)	1568 (19.9)	.076
Functional status			
Independent	430 (96.6)	7714 (98.0)	.100
Partially independent	11 (2.5)	119 (1.5)	
Totally dependent	2 (0.5)	9 (0.1)	
Unknown	2 (0.5)	28 (0.4)	
*BMI			
Underweight	8 (1.8)	77 (1.0)	.006
Normal weight	100 (22.5)	1392 (17.8)	
Overweight	160 (36.0)	2724 (34.8)	
Obese	176 (39.6)	3643 (46.5)	

\*\* eGFR reported as median (Q<sub>1</sub>-Q<sub>3</sub>).

**Table 2.** Complications captured by NSQIP by procedure

Complication grade by Calvien-Dindo index	Dialysis		P Value
	Yes n (%)	No n (%)	
Minor			
Superficial incisional infection	8 (1.8)	81 (1.0)	.147
Pneumonia	10 (2.2)	64 (0.8)	.006
Pulmonary embolus	NA	25 (0.3)	.642
UTI	3 (0.7)	114 (1.5)	.216
Blood transfusion	54 (12.1)	457 (5.8)	<.0001
Deep vein thrombosis	3 (0.7)	36 (0.5)	.464
Total	78	777	
Major			
Deep incisional infection	NA	6 (0.1)	1.00
Organ space wound infection	4 (0.9)	27 (0.3)	.081
Wound dehiscence	3 (0.7)	31 (0.4)	.427
Reintubation	9 (2.0)	58 (0.7)	.009
Ventilator >48 h	3 (0.7)	27 (0.3)	.215
Cardiovascular accident	2 (0.5)	11 (0.1)	.151
Cardiac arrest	5 (1.1)	12 (0.2)	<.0001
Myocardial infarction	6 (1.4)	31 (0.4)	.013
Sepsis	2 (0.5)	34 (0.4)	.719
Total	34	237	
Death	5 (1.1)	35 (0.4)	.061

UTI, urinary tract infection.

\*Only highest grade complication accounted for per patient.

**Table 3.** Complication according to status of dialysis

Complication Grade	Dialysis		P Value
	Yes n (%)	No n (%)	
None	355 (79.8)	7,028 (89.3)	<.0001
Minor	65 (14.6)	639 (8.1)	<.0001
Major	20 (4.5)	168 (2.1)	.0025
Death	5 (1.1)	35 (0.4)	.0605

greater than 4 days than those patients not needing preoperative dialysis (27.2% vs 16.5%,  $P < .0001$ ).

The results of the multivariable logistic regression analysis identifying factors associated with perioperative outcomes are displayed in Table 4. The presence of diabetes, CHF (congestive heart failure), ASA score above 3, and preoperative dialysis were all associated with an increasing risk of complications postoperatively. Patients needing preoperative dialysis had a higher likelihood of having an adverse perioperative event than those not requiring dialysis (OR = 1.45, CI = 1.08-1.95,  $P = .015$ ). Interestingly, being obese appeared to have an independently protective effect against perioperative events in this analysis (OR = 0.68, CI = 0.55-1.43,  $P = .002$ ).

## DISCUSSION

Our study of 8315 patients who underwent a LRN revealed that patients needing preoperative dialysis had

**Table 4.** Multivariate regression

	Odds Ratio	95% CI	P Value
Sex			
Female	1.00		
Male	0.86	1.01-1.35	.051
Age			
<40	1.00		
40-49	1.03	0.66-1.53	.990
50-59	0.88	0.60-1.28	.487
≥60	1.09	0.77-1.56	.626
Race			
Caucasian	1.00		
African American	0.93	0.73-1.19	.557
Asian	0.88	0.54-1.43	.601
Other	0.82	0.32-2.09	.672
Preoperative renal failure	1.45	1.08-1.95	.015
Diabetes	1.29	1.08-1.54	.006
CHF	2.38	1.36-4.16	.002
Hypertension	1.17	0.98-1.40	.083
ASA Status			
≤3	1.00		
4	2.19	1.71-2.80	<.0001
5	N/A	N/A	N/A
Smoking	0.83	0.68-1.02	.075
Functional status			
Independent	1.00		
Partially independent	2.82	1.84-4.33	<.0001
Totally dependent	N/A	N/A	N/A
BMI			
Normal	1.00		
Underweight	0.55	0.24-1.23	.144
Overweight	0.90	0.73-1.10	.298
Obese	0.68	0.55-1.43	.002

ASA, American Society of Anesthesiologists.

higher rates of adverse perioperative events compared to those patients not requiring preoperative dialysis. Statistically significant higher rates of minor and major complications were noted in the dialysis-dependent group. We also found higher rates of blood transfusions, unplanned reintubations, and unplanned return to the operating room in the 30-day postoperative period for the LRN group. LOS was also significantly longer for the dialysis-dependent group as compared to the control group, however this postoperative outcome may be inherently biased since many dialysis patients may have required longer stays in the hospital due to their dialysis requirements or schedule.

Our findings are well-supported by the literature on this topic. A study utilizing NSQIP data from 2005 to 2008 looked at over 165,000 patients who underwent major general surgeries. Of these patients, 1506 or 0.9% were dialysis-dependent. The dialysis-dependent patients had higher overall complications, higher rates of return to the operating room, and longer LOS. These complications were broken down into higher rates of pulmonary complications including pneumonia, unplanned intubation, and ventilator dependence as well as higher rates of death.<sup>16</sup>

With all the aforementioned complications and adverse outcomes in this patient population, one may question the need for performing LRN in this patient population. Research suggests that end stage renal disease (ESRD) patients have higher rates of renal masses, however these masses seem to appear to have a more indolent course than renal tumors in nondialysis patients. In a study of 1250 patients with RCC, T stage, metastatic disease, nodal invasion, and Fuhrman nuclear grade were all statistically significantly lower in the ESRD patient population compared to non-ESRD patient population. Finally, cancer-specific mortality rates were lower in the ESRD patient population.<sup>17</sup>

Traditionally, the predominant histologic subtype in the ESRD population has been reported as papillary RCC. However, a recent study of 27 patients with ESRD who underwent a radical nephrectomy between 1994 and 2008 found lower rates of papillary RCC. This study found the most common tumor type to be acquired cystic disease (ACD)-associated RCC accounting for 44% of the tumors. Papillary RCC was identified in only 11% of the tumors.<sup>18</sup> A separate study of 66 renal masses in ESRD patients revealed papillary RCC to constitute only 12 of 66 (18%) of the tumors while ACD-associated RCC comprised 24 of 66 (36%) of the tumors.<sup>19</sup>

Others have looked at the clinical significance of ACD-associated RCC. In a recent study of 40 patients with ACD-associated RCC, clinical follow-up was available for 36 patients with a mean follow-up length of 27 months. The vast majority 32 of 36 (89%) had no evidence of disease on follow-up. This included 24 patients (67%) who were alive with no evidence of disease recurrence, 4 patients (11%) who were deceased from other causes, and 4 patients (11%) who had died of unknown causes. Four patients did have recurrences, with 2 patients (6%) having local recurrences and 2 patients (6%) developing

metastases. Of the 4 patients with recurrence, 3 out of 4 were staged at pT3a. Three of 4 tumors were International Society of Urological Pathology (ISUP) grade 3 while the remaining tumor was ISUP grade 4.<sup>20</sup> While the true nature of ACD-associated RCC necessitates further study, the low metastatic potential of renal masses found in the ESRD patient population seems well-supported.<sup>21</sup> Nevertheless, given the data suggesting that ESRD patients have a biologically less aggressive form of kidney cancer, it is important to remember that many patients will develop papillary and clear cell tumors that will act in a similar manner to the non-ESRD population.

Given the known higher mortality and morbidity rate of operating on the dialysis-dependent patient as well as lower T stage and Fuhrman grade noted in those found to have a renal mass, some urologists may question the necessity of or timing of treatment. Data are lacking as to the long-term outcomes of active surveillance in the small renal mass dialysis-dependent patient population. A recent survey of active transplant centers in the United States revealed that 59% of participants felt that the preferred treatment entailed a radical nephrectomy followed by active surveillance in 21.3% of the respondents. Of the correspondents whose institutions did not allow active surveillance, 77.4% would monitor small renal masses following transplantation if shown safety of active surveillance.<sup>22</sup>

There are several limitations to our study. The NSQIP database collects patient information up to 30 days following surgery. Complications, including deaths, which occur after this period are not collected, potentially underestimating adverse events. In addition, there are no pathologic variables abstracted thus limiting our ability to comment on the indolence versus aggressiveness or types of tumors seen in this patient population as well as the indications for surgery. Finally, there is an inherent limitation in all large, administrative databases in that we are dependent on the accurate and reliable input of the data. Nevertheless, despite these acknowledged limitations of the data, the size of this dataset and the unique clinical variables collected allow for the examination of clinical scenarios as presented in this manuscript.

## CONCLUSIONS

Our study of over 8000 patients appears to demonstrate that the dialysis-dependent patient population is complex and faces higher morbidity and mortality rates when compared to nondialysis-dependent patients undergoing a LRN. The true aggressiveness of ACD-associated RCC has not been well-defined but seems to be more indolent in nature compared to spontaneous renal masses in the non-ESRD population. With the higher surgical risks and possibly more indolent nature of renal masses in this patient population, the role of active surveillance or delayed nephrectomy until after successful renal transplantation may be a more prudent approach.

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