Risk of End Stage Kidney Disease after Radical Cystectomy According to Urinary Diversion Type

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Purpose: The risk of renal insufficiency has historically been viewed as a long-term consequence of urinary diversion after radical cystectomy. However, there are little data on the long-term rate of end stage kidney disease after urinary diversion and few studies have compared end stage kidney disease rates by diversion type. In a large, population based cohort we evaluated the risk of end stage kidney disease in patients who received an ileal conduit vs continent urinary diversion after cystectomy for bladder cancer.

Materials and Methods: Using the SEER-Medicare 1992 to 2010 data set we identified 4,015 patients treated with radical cystectomy for bladder cancer, excluding those with preexisting renal disease or clinically significant preoperative hydronephrosis. The outcome of interest was end stage kidney disease stratified by diversion type. We used a Cox proportional hazard model for multivariate analysis controlling for demographic, tumor and comorbidity characteristics.

Results: End stage kidney disease developed in 7.2% of patients, including 84% with an ileal conduit and 16% with continent urinary diversion. Median followup was 34 months (IQR 12–73). On multivariate analysis no increased risk of end stage kidney disease was associated with continent diversion (HR 1.06, 95% CI 0.78–1.44, p = 0.71). Overall the estimated risk at 5, 10 and 15 years was 8.3% (95% CI 7.1–9.5), 16.9% (95% 14.6–19.2) and 24.4% (95% CI 20.3–28.5), respectively.

Conclusions: No significant difference in the rate of end stage kidney disease was identified when comparing ileal conduits to continent urinary diversion. A significant risk of end stage kidney disease in the long term was identified in patients with post-cystectomy survival beyond 5 years.

Key Words: urinary diversion; kidney failure, chronic; cystectomy; risk; urinary bladder neoplasms

Abbreviations and Acronyms

CD = continent urinary diversion
CKD = chronic kidney disease
ESKD = end stage kidney disease
GFR = glomerular filtration rate
IC = ileal conduit
SEER = Surveillance, Epidemiology and End Results

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RADICAL cystectomy remains the standard of care in patients with muscle invasive bladder cancer. In the United States IC (80% to 90%) and CD (10% to 20%) represent the most common forms of urinary diversion.[1–3] Renal function is routinely evaluated preoperatively. Results may influence the choice of urinary diversion for a number of reasons with renal insufficiency often cited as a contraindication to CD.[4] The risk of renal insufficiency has historically been viewed as a potential long-term consequence of urinary diversion due to the risk of obstructive uropathy

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secondary to ureteral-enteric anastomotic stricture or disease recurrence, toxin resorption through the bowel segment into the bloodstream to be filtered anew by the kidney and upper tract disease recurrence resulting in surgical removal. As a result post-cystectomy guidelines recommend continued screening of serum creatinine to monitor for renal insufficiency regardless of the choice of urinary diversion.[5]

Previous groups characterized the risk of renal impairment in patients with IC[6] or CD[7,8] in retrospective, single institution studies. While these studies give some insight into the risks of urinary diversion, many provide a limited description of the definition of renal deterioration. Furthermore, in most of the studies serum creatinine or radiological changes served as a proxy for renal deterioration with no true evaluation of changes in the glomerular filtration rate or clinically relevant renal deterioration. Finally, since ESKD requiring dialysis is a relatively infrequent problem after cystectomy, there is a relatively limited number of events at any single institution, precluding a multivariate model to control for confounders. As a result there are little data to characterize the renal function risks of urinary diversion.

While previous groups evaluated varying degrees of kidney function, there are sparse data in the literature on the risk of ESKD after urinary diversion. We evaluated the risk of ESKD in patients who underwent cystectomy in the setting of bladder cancer and determined differences in ESKD development by diversion type.

MATERIALS AND METHODS

Data Source

The linked SEER-Medicare database was used for this study. SEER is a NCI (National Cancer Institute) program that collects information on patients with cancer in the United States. Coupled with the Medicare file, which contains information on health services rendered to eligible patients, this database includes approximately 26% of the American population.[9] It is considered representative of the United States by demographic composition, cancer incidence and mortality. Details on this method of linkage in this database were previously described.[10]

Cohort Selection and Study Population

We identified 9,057 patients diagnosed with urothelial cell carcinoma of the bladder who were treated with radical cystectomy between 1992 and 2010. Excluded from analysis were 40 patients initially diagnosed at autopsy or in a nursing home, 2,210 enrolled in a health maintenance organization, 32 diagnosed in Louisiana in 2005, 1,337 with preexisting chronic kidney disease or prior dialysis, 1,198 with hydronephrosis requiring a urological procedure and 225 with missing socioeconomic variables. This process resulted in a cohort of 4,015 patients. Study outcomes were reviewed until patient death or the study end on December 31, 2011.

Variables

We report age at radical cystectomy, gender, race/ethnicity and SEER tumor registry region as classified by the United States Census Bureau. Socioeconomic measures (income and education) were accessed at the census tract level. Disease stage was based on SEER recoded extent of disease as Ta, Tis, T1, T2, T3, T4 or unknown. Tumor grade was recorded as specified in the SEER registry as low, medium, high, undifferentiated/anaplastic or unknown. The adaptation by Klabunde et al[11] of the method of Deyo et al[12] was used to calculate the Charlson comorbidity score[13,14] using hospital claims to determine the number of significant comorbid conditions in a patient in the 12 months before cystectomy. Subsequently the men were ordered according to the number of listed comorbid conditions as 0, or 1 or greater.

We used ICD-9 diagnosis codes to identify the diagnosis of various conditions. ICD-9, procedure and CPT codes were used to identify procedures and services received by patients (supplementary Appendix, http://jurology.com/).

The patient was the unit of analysis. The primary outcome of analysis was the development of ESKD. This was considered a diagnosis of stage V CKD as defined by NKF (National Kidney Foundation),[15] the receipt of dialysis (3 consecutive dialysis episodes 30 days apart) or coding of ESKD by billing data. Secondary outcomes were cancer specific and all-cause mortality.

Statistical Analysis

We evaluated univariate descriptive statistics and CD trends. Unadjusted associations between patients who received IC and those who received CD were examined. Statistical inferences were made using chi-square analysis. Univariate Kaplan-Meier analysis of risk of ESKD by diversion type was completed. We applied a Cox proportional hazard model to determine the adjusted effect of covariates on the risk of ESKD. SAS®, version 9.3 was used for analysis with $p < 0.05$ considered statistically significant.

RESULTS

Mean $\pm$ SD age of the cohort was 74.7 $\pm$ 5.5 years. Of the patients 3,364 (83.8%) received IC and 651 (16.2%) received CD. ESKD developed in 290 patients (7.2%) during the study period. Median followup was 34 months (IQR 12–73) and 369 patients had at least 10 years of followup.

Supplementary table 1 (http://jurology.com/) shows a demographic comparison of patients who received IC vs CD. Older patients and women were more likely to receive IC than younger patients and men, respectively ($p < 0.001$). No significant difference was noted in diversion type by race, or tumor stage or grade. Patients with a higher Charlson comorbidity score were less likely to receive CD ($p < 0.0001$).