Trends in Renal Function After Radical Cystectomy and Ileal Conduit Diversion: New Insights Regarding Estimated Glomerular Filtration Rate Variations

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Abstract

We evaluated the long-term natural history of renal function after radical cystectomy and ileal conduit diversion in 226 patients. The median estimated glomerular filtration rate (eGFR) decreased from 66 mL/min/1.73 m^2 to 59 mL/min/1.73 m^2. The strongest predictor of an eGFR decline was CKD stage 1 or 2 (> 60 mL/min/1.73 m^2).

Introduction: Our objectives were to evaluate the long-term renal function after radical cystectomy (RC) and ileal conduit diversion (ICD) and to analyze year-by-year the estimated glomerular filtration rate (eGFR) and morphologic upper urinary tract changes. **Patients and Methods:** We retrospectively identified 226 patients who had undergone RC and ICD from 1980 to 2008, with regular postoperative follow-up visits. The eGFR was calculated using the Modification of Diet in Renal Disease equation at baseline and during follow-up. A decrease in renal function was defined as $>$ 1 mL/min/1.73 m^2 annually. **Results:** The median follow-up period after RC was 91 months (range, 61-235 months). The median eGFR decreased from 66 mL/min/1.73 m^2 (range, 17-139 mL/min/1.73 m^2) to 59 mL/min/1.73 m^2 (range, 33-102 mL/min/1.73 m^2). A rapid decline in renal function occurred during the first 2 postoperative years ($-$9 mL/min/1.73 m^2 and $-$4 mL/min/1.73 m^2 in the first and second year, respectively), with a moderate to slight decrease in the subsequent years. Urinary obstruction was diagnosed in 51 patients (23%). Among the patients who underwent prompt surgical treatment, we did not find any association with the eGFR decline ($P = .8$).

Conclusion: Patients with urinary ICD have a lifelong risk of chronic kidney disease. Regular monitoring of renal function and the morphologic upper urinary tract will permit early diagnosis and treatment of modifiable factors, avoiding irreversible kidney damage.

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Introduction

Since the past decade, chronic kidney disease (CKD) has been identified as an independent risk factor of death, cardiovascular events, and use of specialized healthcare.[1] Arguably, commonly used drugs and surgical intervention can adversely affect several aspects of kidney function. Therefore, physicians should be aware of the renal function variations that can occur after medical intervention.

Although it remains the reference standard treatment of muscle-invasive and high-risk urothelial bladder carcinoma, radical cystectomy (RC) is associated with significant risks of perioperative and long-term morbidity and mortality, notably due to renal function impairement.[2,3] Despite the variety of diversion techniques, either continent or noncontinent, patients undergoing RC have a life-long risk of CKD. Several factors have been identified to explain the renal function decrease, including nonmodifiable parameters such as age, the nephrotoxicity of chemotherapy or medical treatment, chronic hypertension, and diabetes mellitus, and potentially modifiable factors, including mechanical obstruction and urinary tract infection.[4]

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However, the natural history and long-term follow-up data of renal function decline in patients treated by RC for urothelial bladder cancer have been poorly reported.[5,6] Furthermore, most of the studies have evaluated renal function variations using serum creatinine as a surrogate value for the estimated glomerular filtration rate (eGFR). Although the reference standard for renal function evaluation is the measured GFR, equations estimating the GFR have been considered to be the better measure of overall kidney function in routine clinical practice.[7]

In the present study, we analyzed the year-by-year eGFR variations and morphologic upper urinary tract changes in patients who had undergone RC and urinary ICD for urothelial bladder cancer.

Patients and Methods

Patient Selection

From January 1980 to December 2008, 903 consecutive patients had undergone RC for localized muscle-invasive bladder cancer at our tertiary referral urologic cancer center. Of these patients, 579 (64%) underwent orthotopic ileal neobladder diversion and 295 (33%) underwent ICD. Those patients with a preoperative eGFR < 15 mL/min/1.73 m^2, cutaneous ureterostomy, and ureterosigmoidostomy were not included. The clinical variables evaluated included age, gender, diabetes mellitus, preoperative chronic hypertension, body mass index, American Society of Anesthesiologists class, preoperative hydronephrosis, baseline and follow-up eGFR, and receipt of perioperative systemic chemotherapy. Our institutional review board approved the present study.

Surgical Technique

All patients underwent pelvic lymphadenectomy before RC was performed. An ileal segment 5- to 10-cm long was isolated approximately 20 cm proximal to the ileocecal valve. The ureters were split and anastomosed separately in the ileal segment. Ureteroileal anastomoses were performed using either direct implantation (51%) or the Wallace technique (49%). The ureteral catheter was brought directly through the ileal segment and secured to the abdominal skin. The ileal segment was oriented in the isoperistaltic direction and anastomosed to the abdominal wall in a nipple-to-stoma fashion. The ureteral catheters were removed on the 11th or 12th postoperative day.

Patient Follow-Up Data and Data Collection

The patients were followed up regularly at our department or their local hospital at 1, 3, and 6 months, then every 6 months for ≤ 5 years, and annually thereafter. For patients followed up elsewhere, the data were obtained from their local hospitals or by interviewing their general practitioner. At each visit, the patients' blood pressure, complete blood count, serum creatinine, and urine culture were determined. Renal ultrasonography or abdominopelvic computed tomography were performed alternatively every 6 months for 2 years and annually thereafter. The radiologists diagnosed hydronephrosis by measuring the anteroposterior diameter of the renal pelvis. The images of the upper urinary tract were compared with previous images to determine the presence of any radiologic changes. We focused our evaluation on postoperative complications, including mechanical urinary obstruction, urinary tract infection, and urolithiasis. Urinary tract obstruction was documented in patients with hydronephrosis secondary to ureteroileal stricture and/or stomal obstruction. Patients underwent repeat surgery, and the obstruction resolved. The designation of recurrent urinary tract infection was determined by bacteriuria of $\geq 10^5$ colony-forming units lasting ≥ 3 months per year, whether or not symptomatic. Pyelonephritis was defined as a febrile episode with a positive urine culture after excluding another cause for the fever.

Renal Function Evaluation

The GFR was the primary outcome measure. It was calculated using the Modification of Diet in Renal Disease (MDRD) equation[8]: GFR (mL/min/1.73 m^2) = 175 × (serum creatinine) − 1.154 × (age) − 0.203 × (0.742, if female). To be consistent with previous studies, decreased renal function was defined as a reduction in the GFR > 1 mL/min/1.73 m^2 annually after surgery.[4,5,9,10] To evaluate the factors associated with an eGFR decrease, we compared the preoperative values with those obtained at the subsequent postoperative visits. The CKD stage was also used to classify renal function.[11] Similar to a recent analysis,[5] we compared the preoperative eGFR with the values obtained at the subsequent postoperative visits. At the 1-year postoperative point, we evaluated serum creatinine, measured 9 to 18 months postoperatively. In addition, we accounted for all subsequent values obtained within 6 months of the following years. The median serum creatinine values were calculated if multiple values were available for a given measurement point.

Statistical Analysis

Continuous, normally distributed and non-normal distributed variables are reported as the median and range. Univariate statistical analyses were performed with Student's *t* test for quantitative variables and Fischer's exact test for qualitative variables. Linear regression analysis was used to test the liaison between the quantitative variables. For all statistical analyses, a 2-sided *P* value $< .05$ was considered statistically significant. All data were analyzed using the Statistical Package for Social Sciences, version 16.0 (SPSS, Chicago, IL).

Results

Patient Characteristics

The clinicopathologic features of the patients at surgery are reported in Table 1. Of the 295 patients, 226 (76.7%), with serum creatinine measurements available at baseline and regular follow-up visits after surgery, were evaluated. The median follow-up period after RC for patients alive at the last visit was 91 months (range, 36-235 months). The overall survival rate was 41% at 5 years. The median patient age was 70 years (range, 43-89 years), and the gender ratio was 3:1. Of the 226 patients, 65 (29%) received platinum-based chemotherapy. Postoperative complications included ureteroenteric stricture (n = 26), stomal stenosis (n = 4), recurrent urinary tract infection (n = 20), pyelonephritis (n = 25), and urolithiasis (n = 27).

Changes in eGFR

Figure 1 shows the median eGFR evolution from baseline to event analysis. At 5 years postoperatively, a decrease in eGFR > 1 mL/min/1.73 m^2 annually was documented in 115 patients