



Short-term Change in Renal Function in Patients Undergoing Continent vs Noncontinent Urinary Diversions

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Submitted January 21, 2013 - Accepted for Publication February 19, 2013

ABSTRACT

Introduction: Despite good supporting evidence, the dogma still exists that patients with renal insufficiency are not good candidates for continent diversions. In this paper, we attempt to evaluate this relationship and investigate the short-term effects of continent and noncontinent diversions on patients with both normal renal function and preexisting renal insufficiency.

Methods: From Sept 2004 to June 2009, 212 adult patients underwent radical cystectomy and intestinal urinary diversion by a single surgeon (SD). Forty-four were excluded secondary to inadequate follow-up (41) or other factors leading to renal compromise (3). Continent diversions were performed either with a Studer orthotopic ileal neobladder (ONB) or a catheterizable stoma with right colon pouch. Evaluation of renal function included pre- and postoperative serum creatinine, bicarbonate, and estimated glomerular filtration rate (eGFR) using the National Kidney Foundation (MDRD) equation. A multivariable linear regression model was used to assess the influence of different urinary diversions on the change in renal function.

Results: Median follow-up for the 168 patients was 18.7 months (3 to 60 months). Forty-four patients underwent ileal conduit and 124 underwent continent diversion (109 ONBs; 15 continent cutaneous diversions). The mean preoperative eGFR between the conduit and continent groups was 63.8 and 73.3, respectively ($P < 0.001$). The mean decrease in eGFR between the 2 groups was -4.1 and -10.3, respectively ($P = 0.41$). In patients with preexisting renal insufficiency, the mean change in eGFR was 1.7 and -0.49, respectively ($P = 0.49$).

Conclusions: The mean change in eGFR, creatinine, and bicarbonate levels following urinary diversion with either conduit or continent diversions were not statistically different in patients with normal or preexisting renal insufficiency at short-term follow-up. This data suggests that mild preexisting renal insufficiency may not be a contraindication to continent diversion.

INTRODUCTION

Patients with lower urinary tract cancers or severe functional or anatomic abnormalities of the bladder often require urinary diversion to prevent pathological complications of the upper urinary tract and/or malignancy progression [1]. The type of urinary diversion selected for each patient depends on several clinical factors, as well as the patient's preference and understanding of the short-term and long-term complications of each. Adequate renal function is necessary to blunt the potential

metabolic side effects of urinary diversion (i.e., hyperchloremic metabolic acidosis), and patients with poor renal function are thought to be less capable of handling the sequelae from these derangements (e.g., bone demineralization, impaired growth, infection, and urolithiasis) [2-4]. This relationship may be exacerbated in continent diversions given the longer urine retention time and the potential for even greater reabsorption of normally excreted products (e.g., NH_4^+).

There is now a growing body of evidence suggesting that

KEYWORDS: Ileal conduit, orthotopic neobladder, renal function, urinary diversion

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CITATION: *UroToday Int J.* 2013 April;6(2):art 20. <http://dx.doi.org/10.3834/uij.1944-5784.2013.04.07>

patients with adequate baseline renal function can tolerate both continent and non-continent urinary diversions without significantly different declines in renal function [2,5-8]. However, in patients with renal insufficiency, the long-term effects of continent versus non-continent diversions on renal function have not been well characterized. Despite this, the 2007 World Health Organization (WHO) consensus conference on bladder cancer concluded that renal compromise (whether due to long-standing obstruction or chronic renal failure), defined as serum creatinine of > 150 to $200 \mu\text{mol/L}$ (~ 1.7 to 2.3 mg/dL), is an absolute contraindication to continent urinary diversion [2].

Conversely, other sources state that patients with normal urine protein levels and a preoperative serum creatinine of $< 2.0 \text{ mg/dL}$ usually do well with intestinal urinary reservoirs [9], and that some patients may actually have reversible renal impairment secondary to the removal of obstruction, inferring that a SCr of $< 2 \text{ mg/dL}$ may not be a necessary prerequisite.

The intent of this study is a retrospective review of renal function following urinary diversion in a single institution. We attempt to evaluate the short-term differences in renal function in patients undergoing continent vs non-continent urinary diversions in order to assess the capacity to handle continent urinary diversions in patients with renal insufficiency. Our cohort is somewhat unique in that patients with mild renal impairment were allowed to undergo a continent diversion.

METHODS

We conducted a single-center, retrospective chart review of 212 consecutive patients who underwent radical cystectomy and urinary diversion by a single surgeon (SD) between September 2004 and July 2009 at Oregon Health Sciences University in Portland, OR (IRB#00004701). This cohort represents 99% of urinary diversions performed at OHSU during this time period. Clinical variables reviewed included age, gender, race, indications for surgery, the type of urinary diversion performed, the length of follow-up, evidence of preoperative urinary obstruction (via CT, MRI, or chart-note verification as appropriate), whether patients underwent perioperative chemotherapy, and preoperative and postoperative plasma creatinine and bicarbonate levels. For assessing renal function, labs at the most recent follow-up visit at the time of data analysis were included. Continent diversions were performed either with a Studer orthotopic ileal neobladder (ONB) using a 60 cm segment of distal ileum or a cutaneous diversion with a right colon pouch via Monti or appendicoumbilicostomy. Ureteroileal anastomoses were performed individually using the Leadbetter-Clarke method with interrupted absorbable sutures.

Indications for cystectomy and urinary diversion included

bladder cancer (203, 96%), prostate cancer (2, 0.01%), and other assorted causes (7, 3%). Evaluation of renal function included pre- and postoperative serum creatinine (SCr), bicarbonate (HCO_3), and estimated glomerular filtration rate (eGFR, calculated using the Modification of Diet and Renal Disease (MDRD) equation, which incorporates age, gender, race, and serum creatinine). Subgroup analyses included short-term (3 to 12 months) versus longer-term follow-up (> 1 year) ($N = 58$ vs $N = 110$, respectively), continent versus noncontinent diversion ($N = 124$ vs $N = 44$, respectively), and the presence of preexisting renal insufficiency (58 with RI vs 110 with normal renal function). For the purposes of this study, we chose an eGFR between 40 to 59 (mild to moderate, stage III CRF) as our definition of "renal insufficiency" and any patients with eGFR > 60 as "normal."

Each patient undergoing urinary diversion was given extensive preoperative counseling and a standardized presentation of available options, including a 12-page illustrated handout describing the different diversions in detail. Contraindications for continent diversion included SCr of $> 1.8 \text{ mg/dL}$ ($159.12 \mu\text{mol/L}$) or an eGFR of $< 40 \text{ mL/min } 1.73 \text{ m}^2$, unforeseen pelvic spread of disease (clinical stage T4bNx or TxN3), preexisting urinary incontinence, a history of pelvic irradiation, positive urethral margin at intraoperative frozen section analysis, urethral stricture, hepatic dysfunction, and neurological disease.

Multivariable analysis was used to assess the influence of different urinary diversions on renal function change while controlling for potential confounding effects of clinical factors, including age, preoperative renal function, preoperative obstruction, and perioperative chemotherapy using statistical software SAS (version 9.2). Differential analysis between groups was performed using the Fisher's exact test. The Tukey-Kramer adjustment for multiple comparisons was used to compare the effects of chemotherapy on postsurgical outcomes.

RESULTS

General Results

The mean follow-up for conduit and continent procedures was 17.5 and 19.9 months, respectively. Forty-four patients were excluded, 41 due to inadequate follow-up (< 3 months) and 3 due to other factors leading to unrelated renal compromise. The resulting 168 cases were made up of 44 ileal conduits, 109 ONBs, and 15 continent cutaneous diversions. Of those patients eligible for continent urinary diversion, 9 (6%) chose ileal conduit for personal reasons, which varied significantly and included fear of any incontinence, unwillingness to self-catheterize, belief it was "too complicated," and concern that catheterizing a continent cutaneous pouch would interfere with outdoor activities. A total of 11 patients from the cohort

Table 1. Clinical characteristics of cohort. eGFR of patients with preexisting renal insufficiency (defined as eGFR < 60 mL/min/1.73 m²) calculated using MDRD equation.

| | Conduit (44) | Continent (124) | Significance |
|---------------------------|--------------|-----------------|-------------------|
| Average age | 71.4 | 65.3 | <i>P</i> < 0.001* |
| Mean preop eGFR | 63.8 | 73.3 | <i>P</i> < 0.001* |
| Preop hydronephrosis (54) | 16 (36%) | 38 (31%) | <i>P</i> = 0.6 |
| Periop chemotherapy (44) | 11 (25%) | 33 (75%) | <i>P</i> = 0.52 |
| Preexisting RI (58) | 24 (41%) | 34 (59%) | <i>P</i> = 0.02* |
| Mean preop eGFR with RI | 41 | 48.5 | <i>P</i> < 0.009* |
| | Conduit | Continent | |
| Mean f/u for all | 17.5 months | 19.9 months | <i>P</i> = 0.10 |

RI = renal insufficiency; * denotes significance

underwent an ileal conduit solely based on renal insufficiency (SCr of > 1.8 mg/dL (159.12 umol/L)) and 3 based on surgeon discretion due to comorbidities [10]. Looking at all patients undergoing conduit procedures, this group was significantly older than those undergoing continent diversions (71.4 vs 65.3, *P* < 0.001) and had lower mean preoperative eGFRs (63.8 vs 73.3, *P* < 0.001). Fifty-four patients presented with preoperative obstruction (hydronephrosis) and 44 underwent perioperative chemotherapy. In the patients with renal insufficiency (RI), there was a significant difference of a mean preoperative eGFR between conduit and continent diversions (41 vs. 48.5, *P* < 0.009), and significantly more patients with renal insufficiency underwent conduit diversions (*P* = 0.02) (Table 1).

Postoperative Analysis

For postoperative analysis, we examined the length of follow-up in relation to the type of diversion to evaluate whether there was an initial decline followed by stabilization or the possibility of improved renal function after obstruction correction. Of the 168 cases, there were 58 with short-term follow-up (3 to 12 months) and 110 with longer-term follow-up (> 1 year). The patients with conduit diversion in the short-term group experienced a small increase in renal function (eGFR: +1.6) while the continent group experienced a decline (eGFR: -9.3). These differences, however, were not statistically significant (*P* = 0.35). The longer-term group experienced a decline in

Table 2. Renal function changes after surgery in the 2 general diversion types (ileal conduit vs ONB or continent cutaneous diversion with a right colon pouch). Serum creatinine shown in mg/dL and (umol/L).

| Patients | Markers | Changes after Surgery | | P value* |
|--|------------------|-----------------------|------------|----------|
| | | Conduit | Continent | |
| All (N = 168) | Creatinine | 0.2 (17.7) | 0.2 (17.7) | 0.56 |
| | HCO ₃ | -0.4 | -1.3 | 0.18 |
| | eGFR | -4.1 | -10.3 | 0.41 |
| Short term f/u (N = 58) (3-12 months) | Creatinine | -0.1 (8.8) | 0.2 (17.7) | 0.054 |
| | HCO ₃ | 0.3 | -1.3 | 0.27 |
| | eGFR | 1.6 | -4.5 | 0.35 |
| Longer term f/u (N = 110) (> 1 year) | Creatinine | 0.4 (35.4) | 0.2 (17.7) | 0.48 |
| | HCO ₃ | -1 | -1.3 | 0.58 |
| | eGFR | -9.3 | -12.7 | 0.96 |
| Normal renal function (N = 110) | Creatinine | 0.1 (8.8) | 0.3 (26.5) | 0.18 |
| | HCO ₃ | -0.1 | -1 | 0.61 |
| | eGFR | -11.1 | -14 | 0.65 |
| Preop insufficiency (eGFR < 60) (N = 58) | Creatinine | 0.2 (17.7) | 0.1 (8.8) | 0.98 |
| | HCO ₃ | -0.6 | -2.1 | 0.13 |
| | eGFR | 1.7 | -0.4 | 0.49 |

*Multivariate analysis corrected for age, renal insufficiency, preoperative obstruction (hydronephrosis), and follow-up time (when appropriate).

renal function for both conduit and continent diversions but these were also not significant changes (*P* = 0.96). None of the changes in serum HCO₃ were statistically significant (Table 2). The ureteroileal anastomotic stricture rate was ~2% (3/168), each of which was repaired at an average of 6 months from initial surgery, all without significant loss of renal function.

Renal Insufficiency

There were 58 patients with mild to moderate renal insufficiency with mean preoperative eGFRs of 41 and 48.5 for ileal conduit and continent diversion groups, respectively. There was no

statistically significant difference in functional renal decline in either group with an 18-month follow-up. The conduit group experienced a small increase in renal function (eGFR: +1.7) while the continent group experienced a negligible decline (eGFR: -0.4) ($P = 0.49$). Both groups showed a decline in serum HCO_3^- with a trend toward a steeper decline in the continent group ($P = 0.13$) (Table 2).

Confounding

We also analyzed the potential confounding effect of renal function improvement secondary to obstruction release. There was no significant difference between conduit and continent diversion in terms of preoperative hydronephrosis (16 conduit and 38 continent diversions, $P = 0.6$). Multivariable analysis corrected for age, renal insufficiency, and follow-up time (when appropriate), and did not show any significant differences when controlled for these variables (Table 2).

Chemotherapy

Of the total 168 patients, there were 146 who had complete data regarding the use of perioperative chemotherapy, and of those, 44 patients underwent neoadjuvant or adjuvant chemotherapy (11 conduit, 33 continent, $P = 0.52$). Blood samples were drawn preoperatively, after neoadjuvant chemotherapy, and at the most recent clinical follow-up. When controlling for age, preoperative eGFR, and preoperative obstruction and chemotherapy, there were again no significant differences seen in terms of SCr, eGFR, and HCO_3^- in the 2 diversion groups (using the Tukey-Kramer adjustment for multiple comparisons). Repeating the analysis of this cohort in terms of normal preoperative eGFR versus the renal-insufficient groups again yielded no significant differences using the same test (data not shown).

DISCUSSION

Urinary diversion is a vital component of treating lower urinary tract malignancies and other anatomic or functional urologic problems. The advancement of surgical techniques combined with increasing surgeon experience has provided several diversion options that can now be offered with few contraindications.

In this study, we measured overall decline in function relative to the type of urinary diversion performed. Our data shows, with relatively short-term follow-up, this type of diversion did not adversely affect renal function in any significant way. These findings are consistent with other recent studies. Osawa et al. [8] studied 70 patients (45 continent, 25 conduits) with a mean follow-up of 47 months and found no difference in renal deterioration between the types of diversion. Hofner et al. [6] examined 224 patients (131 conduits, 94 ONBs) and calculated a

5-year probability of freedom from new onset decline in renal function (de novo eGFR < 60) calculated as 47.8% of conduits and 44.8% of ONBs ($P = 0.73$). Bazzi et al. [5] studied 109 patients (25 continent, 84 noncontinent) with a mean follow-up of 25.6 months, which also showed no significant difference in overall renal decline. Xiao-Dong et al. [11] retrospectively examined a cohort who survived > 10 years after surgery (50 ileal conduits, 111 ONBs), defining renal deterioration as > 10 ml/min eGFR loss in 10 years, and found no significant difference in decline relative to the type of diversion performed. Our data combined with these other studies yields a compelling argument that there is, in fact, no differential adverse effect on renal function when comparing continent and noncontinent diversions in the short term.

This still does not answer the question of whether preexisting renal insufficiency should, in fact, be an absolute contraindication. Many experts quote an SCr of 150 to 200 $\mu\text{mol/L}$ (~ 1.7 to 2.3 mg/dL) as an absolute contraindication to continent diversion despite the paucity of data in the literature. This roughly equates to an eGFR of ~ 30 to 43 ml/min/1.732 in a 65-year-old Caucasian male (stage III CRF). The rationale behind this recommendation is that when poor renal function exists the body will be less capable of handling the additional acid load and metabolic abnormalities, leading to increased comorbidity and possibly mortality. The question remains whether urinary diversion in and of itself leads to further renal function loss. One could argue that patients with poor renal function are much more vulnerable to renal insults, and a continent procedure may be the tipping point into fulminant renal failure. However, this is difficult to isolate given age-related decline (which has been estimated at 1 ml/min/yr in those $> \text{age } 50$) [12] as well as numerous other contributing insults over a lifetime (i.e., HTN, DM).

Patients in this study with mild to moderate renal insufficiency showed no statistically significant difference in renal functional decline in either cohort with an 18-month follow-up. This finding suggests that patients with mild to moderate renal insufficiency may be acceptable candidates for continent diversion. While it is true that patients with continent diversion surgeries are generally younger and need to be motivated, committed, and have the necessary dexterity to care for continent diversion, all else being equal, continent procedures in appropriately selected patients may preserve renal function as well as noncontinent procedures.

While we did not show any significant trends toward adverse effects of continent diversions, the follow-up is still relatively short, and it is perhaps too early to discern whether these observations will stand the test of time. This study was not intended to extrapolate the short-term findings to the long-term results given the fact that so many factors can contribute to functional renal decline over time (age, HTN, DM, infections, etc.). However, the type of diversion does not appear to be

the sole reason for long-term functional decline considering several studies have described functional deterioration with both conduit and continent diversions over the long-term (2,7,11,13-16). In fact, some long-term studies have shown a beneficial effect of continent versus conduit diversion in relation to decline [14] and that other underlying problems (postoperative obstruction, DM, HTN) may be more pertinent to declining renal function rather than the type of diversion performed [11]. Certainly, longer-term follow-up is necessary to assess whether preexisting renal insufficiency affects the outcome of continent diversion surgeries, although up to 40% of patients die from either disease or secondary causes within 5 years following cystectomy, precluding robust long-term studies on renal function [17].

One limitation to this data is that we are using discrete points in time to assess renal function and did not take into account confounding factors such as hydration. Additionally, since this was not a prospective study, there was no assessment protocol for renal function after surgery, and patients had routine follow-up with the most the recent labs at the time of analysis included.

Using the MDRD equation is helpful in establishing an accurate eGFR, but the SCr incorporated into that calculation does not take into account hydration status or other variables out of our control. One could also argue that the MDRD equation is not the most accurate for calculating renal function. However, for this type of analysis, which evaluates the change in values as long as the same equation is used both pre- and postoperatively, the results should be consistent.

We also did not account for hypertension and diabetes within our sample (data unavailable), which certainly plays a role in renal functional decline. However, the sequelae of these comorbidities are better appreciated over the long-term (years) and may not affect short-term data significantly. Additionally, one could also argue that patients who underwent chemotherapy should not be included in an analysis with those who did not. To evaluate this, multivariate analysis was performed (using the Tukey-Kramer adjustment for multiple comparisons), and showed no statistical difference between the 2 groups. Therefore, we felt it was reasonable to include these patients in the analysis.

The number of subjects used in this study is also relatively small, and it is possible there is not enough power to show differential effects on renal function between the 2 surgeries. This is particularly important in regards to the subgroup of renal-insufficient patients (N = 58). As described previously, patients with poor renal function are often considered ineligible for continent diversion and therefore it can be difficult to accrue large numbers of patients for this type of analysis. It is important to keep this in mind while interpreting this data. However, our

results are similar to other published data, albeit also with low numbers for analysis, which lends credence to the assertion regarding preexisting renal insufficiency and continent urinary diversion.

Finally, this is retrospective data, with inherent selection bias for patients undergoing continent diversion. This bias we believe is minimized given that only 11 patients from the entire cohort underwent an ileal conduit solely based on renal insufficiency and 3 based on surgeon discretion [10].

CONCLUSION

In this study, the mean change in eGFR, creatinine, and bicarbonate levels following urinary diversion with either an ileal conduit or continent diversion were not statistically different. This was true even with evidence of preexisting mild to moderate renal insufficiency. Although follow-up is relatively short, this data suggests that mild preexisting renal insufficiency may not be a contraindication to continent diversion. In the future, a multi-institutional study with long-term follow-up may be necessary to truly and definitively evaluate the nature of this relationship.

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