Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Long-term kidney function and mortality after radical cystectomy and ileal conduit formation.

Julio Chevarria (jl.chevarria@gmail.com)
Beaumont Hospital https://orcid.org/0000-0002-4641-6568
Chaudhry A. Ebad
Beaumont Hospital
Mairead Hamill
Beaumont Hospital
Catalin Constandache
Beaumont Hospital
Cliona Cowhig
Beaumont Hospital
Hazel O'Shea
Beaumont Hospital
Sandra Deady
National Cancer Registry
Dilly M Little
Beaumont Hospital
Peter J. Conlon
Beaumont Hospital

Research article

Keywords: Dialysis, chronic kidney disease, Bladder cancer, Cystectomy

Posted Date: October 1st, 2020

DOI: https://doi.org/10.21203/rs.3.rs-57335/v2

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Abstract

Background: Treatment for bladder cancer includes radical cystectomy (RC) and urinary diversion, RC is associated with long-term morbidity, kidney function deterioration and mortality. Our aim was to identify risk factors associated with postoperative long-term kidney function decline and mortality.

Methods: Retrospective study of patients with RC and urinary diversion in Beaumont Hospital from 1996 to 2016. We included patients who had follow up data of at least two years post procedure. We assessed the following outcomes: estimated glomerular filtration rate (eGFR) preoperatively, at first and second year post-procedure, kidney function decline >10 ml/min/1.73m 2 , dialysis commencement and mortality. Logistic regression analyses were applied to assess risk factors associated, a p-value <0.05 was considered significant.

Results: We included 264 patients, with median age 68.3 years, 73,7% males. The most common diagnosis was bladder cancer 93.3%, TNM stages were grouped in T≥2 75.9%, N≥1 47.6% and M1 28%. The median eGFR preoperative was 65.8 ml/min/1.73m 2 and after 2 years 58.2 ml/min/1.73m 2 (p:0.009), 5.6% required chronic dialysis and 32.8% had a decrease >10 ml/min/1.73m 2 . Risk factors associated with ESKD included; age (HR:1.13, CI95% 1.05-1.22), and pre-operative eGFR (HR:1.04, CI95% 1.01-1.07). Overall mortality was 43.2% and 75.9% at 5 and 10 years respectively, risk factors for which were age (HR:1.1, CI95% 1.04-1.18), preoperative eGFR (HR:1.03, CI95% 1.01-1.06) and male gender (HR:14.8, CI95% 1.1-192).

Conclusions: Patients with RC are at risk of progressive kidney function deterioration and elevated mortality and the main risk factors associated were age, sex, and preoperative eGFR. Regular monitoring of kidney function will permit early diagnosis and treatment.

Background

The international gold standard treatment for muscle invasive bladder cancer with curative intent is a multimodal approach involving radical cystectomy (RC), resection of regional lymph nodes, urinary diversion and neo-adjuvant chemotherapy (1). The two most commonly used procedures for urinary diversion are ileal conduit diversion (ICD) and orthotopic neobladder formation (2). Although surgery itself is associated with significant peri-operative morbidity and mortality, the 5-year relative survival rate has improved greatly in recent years (3,4). It has resulted in consideration of the long-term impact of surgery on morbidity, quality of life and it has been shown that patients after RC are at increased lifetime risk of deterioration in kidney function and progression to chronic kidney disease (3–7).

Chronic kidney disease itself is an independent risk factor for all-cause mortality, and cardiovascular events (8,9). Multiple factors have been implicated in the deterioration of kidney function postoperatively, these can be divided into patient factors such as advancing age, central obesity, diabetes mellitus, hypertension, pre-operative kidney impairment, and iatrogenic factors such as use nephrotoxic chemotherapy, perioperative blood loss, post-operative urinary tract infection or obstruction (10–16). The

trajectory of the deterioration of kidney function is thought to be biphasic: an accelerated decline is seen in the first two postoperative years with a moderate loss occurring gradually over later years (12).

In this study, we analysed data from all patients who underwent radical cystectomy in our hospital, a tertiary referral centre for urological cancer, from 1996 to 2016. The aim was to identify potential risk factors associated with postoperative and long-term kidney function decline and mortality.

Methods

Following institutional review board approval, a retrospective study was conducted of patients undergoing radical cystectomy from January 1996 to December 2016. We identified a total of 338 consecutive adult patients underwent radical cystectomy and urinary diversion attended in Beaumont Hospital Urology department. We excluded patients with partial cystectomy (n = 33), without urinary diversion due to dialysis (n = 2) and patients whose analysis data were unavailable or incomplete (n = 39). We included 264 patients who had undergone total radical cystectomy and ileal conduit diversion or cutaneous ureterostomy who had on going assessment for at least two years post procedure, with clinical and laboratory. We confirmed the mortality status with the National Cancer Centre Office database, which is maintained prospectively.

The preoperative factors analysed were age at RC, gender, smoking history, concomitant comorbidity (DM and HTN), body mass index (BMI), preoperative kidney function, type of surgical technique, indication for surgery and tumour stage. The main outcomes were mortality, kidney function deterioration and end stage kidney disease (ESKD). We assessed kidney function using the CKD-EPI equation for estimated glomerular filtration rate (eGFR) (17). Deterioration in kidney function was defined as clinically relevant if there was a >10 ml/min/1.73m^2 decrease in eGFR at 2 years compared to the baseline value before surgery. This threshold was chosen rather than 5ml/min/year because this rate of deterioration has been shown to be superior and is considered more clinically meaningful (14,18).

Data analysis and statistical methods.

Continuous variables are shown using summary statistics and categorical variables as frequencies. We performed exploratory analyses for categorical variables using Fisher's exact or Chi square test and continuous with student's T test. The occurrence of ESKD requiring dialysis was estimated using the Kaplan-Meier method and compared using the Log rank test. Patients who had not experienced the event of interest were censored at the time of the last urologic follow-up or death not owing to events of interest.

Multivariate logistic regression was applied to identify independent risk factors and reported as hazard ratios (HR) with 95% CI. The covariates were selected among baseline variables and compared in a bivariable model, with the patient outcomes of mortality and ESKD. We selected variables to be included in regression models if the p-value was <0.10. We included age, sex and eGFR perioperative in all models.

To achieve model parsimony and stability, we analysed all possible models and selected the best model using the criteria of a change of <10% in the full model B coefficient, and applying a selection procedure based on the dropout criterion of P>0.1. All probabilities were two sided, and a p-value <0.05 was considered significant. All analyses were performed using SPSS 19 (IBM-California).

Results

We evaluated 264 patients, the clinic pathological characteristics and distributions are shown in Table 1. The median age was 68.3 years (IQR 13.7), mean weight was 74.0 kg (SD 20), height 170 cm (SD 11), BMI 25.2 km/m^2 (SD 6.3). 73,7% were males, 14,7% had diabetes, 44.2% HTN, 29.3 IHD, 9% CVA, 18.5% PVD, 30% were smokers and 43.9 ex-smokers. The main indication for surgery was bladder cancer 93.3%, and other 6.7% (haemorrhagic, shrunken bladder, neurogenic). The surgical techniques were Wallace 29.8%, and Bricker 64%. The main postoperative complications were pyelonephritis 6.4%, recurrent UTI 19.1%, Ureteral stricture 7.9%, lithiasis 4.8%, while 12.7% required admission in ICU, 14.3% had surgical infection, 23.4 had sepsis. A total of 75.9% died, and 5.3% started dialysis. Overall pathological T, N and M stage were grouped in T ≥ stage 2 (75.9%), N ≥ stage 1 (47.6%) and M1 stage (28%) (Table 1).

The median eGFR pre-operative was 65.8 ml/min/1.73m^2 (IQR 48.5 to 81.5), and after 2 years decreased to 58.2 ml/min/1.73m^2 (IQR 45.3 to 79.2), the difference being statistically significant (p: 0.009) (Graphic 01). Fourteen patients (5.6%) went on to develop CKD stage V and required chronic dialysis, 2 of whom required dialysis immediately, median time dialysis commencement was 3.3 years (IQR 8.0). 41.3% of patients had moderate to severe CKD (stage III-V) pre surgery; after 2 years postoperatively this percentage increased to 53.9%. A decrease in eGFR greater than 10 ml/min/1.73m^2 at two years was present in 32.8%. It is noteworthy that 63.3% of patients had a reduction in their eGFR after 2 years, although 36.7% maintained stable kidney function or had a mild increase in their eGFR.

In bivariable analysis, independent risk factors for ESKD and commencement of dialysis were age (HR 1.64, CI95% 1.02 - 1.12), stage T≥2 (HR 3.4, CI95% 1.2 - 10.3) and pre-operative eGFR (HR 1.02, CI95% 1.0 - 1.05) (Table 02). The Kaplan–Meier curve showed that the cumulative incidence of ESKD at 5-years was 5.6% (Graphic 02). On logistic regression analysis, both preoperative eGFR (HR 1.04, CI95% 1.01-1.07) and age (HR 1.13, CI95% 1.05-1.22), were significant factors in predicting ESKD, while gender and tumour stage were not significant (Table 03).

Of those who died, survival time after surgery was 4.6 years. Overall mortality was 21.4%, 43.2%, and 75.9% at 1, 5 and 10 years, respectively. In bivariable analyses, independent risk factors for mortality was age (HR 0.94, CI95% 0.92-0.97), male sex (HR 2.0, CI95% 1.2-3.5), bladder cancer (HR 10.1, CI95% 3.4-30.2), and stage T≥2 (HR 2.3, CI95% 1.3-4.2). In logistic regression analysis, older patient age (HR 1.1, CI95% 1.04-1.18), preoperative eGFR (HR 1.03, CI95% 1.01-1.06) and male gender (HR 14.8, CI95% 1.1-192) were independently associated with increase in mortality (Table 04).

Discussion

The demographics of our cohort are similar to that of previous studies in terms of age, gender (10–14,19–21), mean follow up period 7.5 to 10 years (5,11–14,20,21), prevalence of hypertension and diabetes (10–12,14,20,21), indication for RC bladder cancer (10–12,14,19,20), with stages T≥2 from 63 to 78% (12,20,21). Therefore, our study is comparable to these previous reports.

We found that the majority of patients experienced a decrease in kidney function during long-term follow up. The initial eGFR in our cohort was 65.8 ml/min/1.73m^2, which is similar to previous reports (10,12–14,20) with initial eGFR ranging from 65 to 69.7 ml/min, with the exception of Samuel et al, which reported an eGFR of 77. This was most likely due to the fact that the cohort in Samuel et al was younger. The eGFR after two years was 55 ml/min, again similar to previous reports with ranges from 55 to 59 (11–14,20), being comparable. 62.8% of patients had a decline of their kidney function during follow up, and 32.8% of patients had a decrease of >10 ml/min/1.73m^2 at 2 years. Previous studies have shown a high prevalence 70% (11,21) at 10 years, and 49% at 5 years (11), however there are also reports with a lower prevalence 34 to 51% (12–15). The difference in the prevalence across the different studies could be explained by the variety in definitions used to categorize the decline in kidney function, as well as different follow up times, and different methods of GFR estimation.

There is a predictable decline in the kidney function related to aging; the annual age-related decline in eGFR from age 30 years onward is believed to be ±1 mL/min/1.73 m^2 in a healthy population (22–24). This GFR declines by about 8 – 10 ml/min/1.73 m^2 per decade (25,26), however a linear decline in eGFR over time is often observed (27) in patients with diabetes or HTN. This decline in persons with diabetes can range from ±2-3 mL/min/1.73m^2 per year (28). In patients with RC and ICD, previous reports have used definitions such as a decrease of 1 ml/min/year (5,11,12) over a time period of 5 to 10 years, a decrease of >25% (15,20) in eGFR from baseline, or a decline of >10% in eGFR (11,14). The definition of a clinically significant deterioration in kidney function in our study was a decrease of >10 ml/min/1.73m^2 in the first two years. This was selected because the majority of the observed decline in kidney function in previous studies occurs in the first 2 years (12,20). This represents the period of major risk for kidney function deterioration, which is likely associated with RC and of clinical significance.

A further difference relates to the method used to measure kidney function in patients with RC. The most common methods used are the MDRD (12,14,19), CKD-EPI equations (10,11) and isotopic (5,19) methods. These equations represent a practical way to measure kidney function, which is reliable, easy to use and reproducible. The gold standard to measure GFR is the use of isotopes or inulin; these methods are costly and not widely available in clinical practice. There are reports that suggest that methods like MDRD and CKD-EPI overestimate the GFR comparing this with isotopic methods (19) in patients post RC. Therefore, the differences between these series can be explained by variations in patient selection and the variety of methods used to calculate eGFR.

The use of estimated methods to assess the kidney function have some caveats and considerations. One important consideration is that these equations are dependent on the level of serum creatinine; the level of which reflects kidney function but serum creatinine can also be affected by muscle mass, weight, diet,

exercise and other possible factors (29,30). For example, a decrease in body weight after a diagnosis of cancer is a frequent phenomenon, Meyerhardt et al, previously reported a decrease in 37.5% of patients (31). On the other hand, it is unclear whether there is significant reabsorption of urea and creatinine in ICD patients, as the contact time of urine is shorter and the reabsorbing surface of an ICD is small. Animal models suggest that much of the creatinine is reabsorbed by solvent drag, a glucose-dependent way of transport. Creatinine is reabsorbed less well by an active carrier mediated transport. As urine normally does not have large amounts of glucose, creatinine may be resorbed to a lesser degree (32).

It should be noted that changes in kidney function were not uniform across patients, in our analysis we showed that 36.7% of our patients has stable or mild increase in their eGFR, and 10.6% an increase of >10%, since previous reports showed similar findings Rouanne (12) et al 26%, Gondo (10) et al 56%. The presence of clinical or subclinical urinary obstruction (5) can affect kidney function, and release of the ureteral obstruction could lead to an improvement in kidney function (5,10).

Our study showed cumulative incidence of dialysis of 5.6% at 5 years; Jin et al (14), reported only 1.2% and Rouanne (12) et al only 2.5%. The low incidence in the Jin (14) et al report may be related to a younger cohort and patient selection. Additionally, the incidence of dialysis may be affected by high mortality since there is a higher incidence of comorbidity, and conservative treatment may have been adopted rather than dialysis..

Long-term kidney function after RC can be adversely affected by several factors, including age, potential nephrotoxic chemotherapy, comorbidities, and urine diversion-related factors. Our results are concordant with previous studies, in that age and preoperative eGFR associated significantly with postoperative kidney function on both univariate and multivariate analyses (11,12,33). However, there is not a clear consensus about other risk factors; neither chronic hypertension nor diabetes mellitus were associated with the decline eGFR (10,12,20,33), or different types of ureterointestinal anastomoses, such as Bricker and Wallace (12,33) or urinary infection (12), or chemotherapy (20,33). Nonetheless, other reports have shown associations with HTN (5,11,14), Diabetes (14), hydronephrosis post RC (11), urinary infection (5,11,14) and total subcutaneous fat (10).

While mortality at 10 years in the other cohorts was from 59 to 65% (12,14) in our study it was 76.5%. After adjustment in multivariate analysis the main risk factors associated were age, pre operative eGFR and sex. The lack of association with previous well-known risk factors like HTN and DM are most likely related to the follow up, the nature of the cancer and a high mortality rate, that have a high impact as a competing event.

The present study is limited by its retrospective nature, and nonrandomized design and the single centre design may be associated with unknown biases. Additionally, we could not include well-known other clinical factors such as nutrition status due to unavailability of this data. Excluding patients without complete data may have introduced selection bias. Despite these limitations, we have analysed a significant number of patients, with regular follow up, and have confirmed mortality and dialysis status with the National Cancer Centre Office and the National Kidney Registry databases which are regularly

updated and maintained prospectively. We did not evaluate the gold standard measures of inulin clearance or use of isotope measured GFR, and while we recognise the potentially limited accuracy of measuring serum creatinine in this cohort, the use of the eGFR is the standard clinical practice due to simplicity, cost and availability, and eGFR is mainly used for management and therapeutic approach in clinical practice.

Conclusions

In conclusion, our study suggest that a high proportion of patients have some degree of renal impairment prior to RC and ileal conduit which will likely deteriorate in the post-operative period. Preoperative eGFR and age, correlate significantly with early postoperative kidney function deterioration, dialysis and mortality. Therefore, it is critical that from time of diagnosis these patients are optimised as their preoperative eGFR may dictate decisions about chemotherapy choices, their likelihood of requiring dialysis and their survival. Follow-up of postoperative kidney function is critical in order to minimise long-term morbidity and mortality. Finally, further investigation by well-designed prospective studies is necessary to assess the changes of postoperative kidney function decline in patients with bladder cancer.

Declarations

Ethics approval and consent to participate.

The present study was submitted to the ethical committee of the Beaumont Hospital and was approved.

Consent for publication.

Not applicable.

Availability of data materials.

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests.

All authors confirm that they have no conflicts of interest related to this research and the results presented in this paper have not been published previously in whole or part, except in abstract format.

Funding.

This study has no external support and was totally done with own resources.

Authors' Contributions.

Research idea and study design: JCH, PC; data acquisition: MH, CC, HO'S, SD; data analysis/interpretation: JCH, CE, PC, DL, MH; statistical analysis: JCH; supervision or mentorship: DL, PC.

Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

Acknowledgements.

We gratefully acknowledge the contributions of the archive service staff, data managers from Beaumont Hospital and the National Cancer Registry of Ireland for providing us with access to the databases and especially to all the patients that are reflected in this research.

Financial Disclosure.

The authors declare that they have no relevant financial interests, and we didn't receive at any time any payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work.

References

1. Stenzl A, Cowan NC, De Santis M, Kuczyk MA, Merseburger AS, Ribal MJ, et al. Treatment of Muscle-invasive and Metastatic Bladder Cancer: Update of the EAU Guidelines. Eur Urol. 2011 Jun 1;59(6):1009–18.
2. Kassouf W, Hautmann RE, Bochner BH, Lerner SP, Colombo R, Zlotta A, et al. A Critical Analysis of Orthotopic Bladder Substitutes in Adult Patients with Bladder Cancer: Is There a Perfect Solution? Eur Urol. 2010 Sep;58(3):374–83.
3. Shabsigh A, Korets R, Vora KC, Brooks CM, Cronin AM, Savage C, et al. Defining Early Morbidity of Radical Cystectomy for Patients with Bladder Cancer Using a Standardized Reporting Methodology. Eur Urol. 2009 Jan;55(1):164–76.
4. Shimko MS, Tollefson MK, Umbreit EC, Farmer SA, Blute ML, Frank I. Long-term complications of conduit urinary diversion. J Urol. 2011 Feb;185(2):562–7.
5. Samuel Joanne D., Bhatt Rupesh I., Montague Richard J., Clarke Noel W., Ramani Vijay A.C. The Natural History of Postoperative Renal Function in Patients Undergoing Ileal Conduit Diversion for Cancer Measured Using Serial Isotopic Glomerular Filtration Rate and 99mTechnetium-Mercaptoacetyltriglycine Renography. J Urol. 2006 Dec 1;176(6):2518–22.
6. Madersbacher S, Schmidt J, Eberle JM, Thoeny HC, Burkhard F, Hochreiter W, et al. Long-term outcome of ileal conduit diversion. J Urol. 2003 Mar;169(3):985–90.
7. Hautmann RE, de Petriconi RC, Volkmer BG. 25 Years of Experience With 1,000 Neobladders: Long-Term Complications. J Urol. 2011 Jun;185(6):2207–12.

8. Baber U, Gutierrez OM, Levitan EB, Warnock DG, Farkouh ME, Tonelli M, et al. Risk for recurrent coronary heart disease and all-cause mortality among individuals with chronic kidney disease compared with diabetes mellitus, metabolic syndrome, and cigarette smokers. Am Heart J. 2013 Aug;166(2):373-380.e2.
9. de Jager DJ, Vervloet MG, Dekker FW. Noncardiovascular mortality in CKD: an epidemiological perspective. Nat Rev Nephrol. 2014 Apr;10(4):208–14.
10. Gondo T, Ohno Y, Nakashima J, Hashimoto T, Nakagami Y, Tachibana M. Preoperative determinant of early postoperative renal function following radical cystectomy and intestinal urinary diversion. Int Urol Nephrol. 2017 Feb;49(2):233–8.
11. Eisenberg Manuel S., Thompson R. Houston, Frank Igor, Kim Simon P., Cotter Katherine J., Tollefson Matthew K., et al. Long-Term Renal Function Outcomes after Radical Cystectomy. J Urol. 2014 Mar 1;191(3):619–25.
12. Rouanne M, Perreaud A, Letang N, Yonneau L, Neuzillet Y, Hervé J-M, et al. Trends in Renal Function After Radical Cystectomy and Ileal Conduit Diversion: New Insights Regarding Estimated Glomerular Filtration Rate Variations. Clin Genitourin Cancer. 2015 Jun;13(3):e139–44.
13. Nishikawa M, Miyake H, Yamashita M, Inoue T, Fujisawa M. Long-term changes in renal function outcomes following radical cystectomy and urinary diversion. Int J Clin Oncol. 2014 Dec 1;19(6):1105–11.
14. Jin X-D, Roethlisberger S, Burkhard FC, Birkhaeuser F, Thoeny HC, Studer UE. Long-term Renal Function After Urinary Diversion by Ileal Conduit or Orthotopic Ileal Bladder Substitution. Eur Urol. 2012 Mar 1;61(3):491–7.
15. Osawa T, Shinohara N, Maruyama S, Oba K, Abe T, Maru S, et al. Long-term renal function outcomes in bladder cancer after radical cystectomy. Urol J. 2013;10(1):784–9.
16. Ku JH, Lerner SP. Variables Affecting Long-term Maintenance of Renal Function Following Ileal Based Urinary Diversion. Eur Urol. 2012 Mar 1;61(3):498–500.
17. Levey AS, Stevens LA. Estimating GFR Using the CKD Epidemiology Collaboration (CKD-EPI) Creatinine Equation: More Accurate GFR Estimates, Lower CKD Prevalence Estimates, and Better Risk Predictions. Am J Kidney Dis Off J Natl Kidney Found. 2010 Apr;55(4):622–7.
18. Levin A, Stevens PE. Summary of KDIGO 2012 CKD Guideline: behind the scenes, need for guidance, and a framework for moving forward. Kidney Int. 2014 Jan;85(1):49–61.
19. Robinson R, Tait CD, Somov P, Lau MW, Sangar VK, Ramani VAC, et al. Estimated glomerular filtration rate is unreliable in detecting renal function loss during follow-up after cystectomy and urinary diversion. Int Urol Nephrol. 2016 Apr 1;48(4):511–5.
20. Makino K, Nakagawa T, Kanatani A, Kawai T, Taguchi S, Otsuka M, et al. Biphasic decline in renal function after radical cystectomy with urinary diversion. Int J Clin Oncol. 2017 Apr 1;22(2):359–65.
21. Gershman B, Eisenberg MS, Thompson RH, Frank I, Kaushik D, Tarrell R, et al. Comparative impact of continent and incontinent urinary diversion on long-term renal function after radical cystectomy in

patients with preoperative chronic kidney disease 2 and chronic kidney disease 3a. Int J Urol. 2015;22(7):651–6.

22. Derose SF, Rutkowski MP, Crooks PW, Shi JM, Wang JQ, Kalantar-Zadeh K, et al. Racial Differences in Estimated GFR Decline, ESRD, and Mortality in an Integrated Health System. Am J Kidney Dis. 2013 Aug 1;62(2):236–44.
23. Peralta CA, Katz R, DeBoer I, Ix J, Sarnak M, Kramer H, et al. Racial and Ethnic Differences in Kidney Function Decline among Persons without Chronic Kidney Disease. J Am Soc Nephrol. 2011 Jul 1;22(7):1327–34.
24. Granerus G, Aurell M. Reference values for 51Cr-EDTA clearance as a measure of glomerular filtration rate. Scand J Clin Lab Invest. 1981 Jan 1;41(6):611–6.
25. Davies DF, Shock NW. The variability of measurement of inulin and diodrast tests of kidney function. J Clin Invest. 1950 May;29(5):491–5.
26. Rowe JW, Andres R, Tobin JD, Norris AH, Shock NW. The Effect of Age on Creatinine Clearance in Men: A Cross-sectional and Longitudinal Study. J Gerontol. 1976 Mar 1;31(2):155–63.
27. Warren B, Rebholz CM, Sang Y, Lee AK, Coresh J, Selvin E, et al. Diabetes and Trajectories of Estimated Glomerular Filtration Rate: A Prospective Cohort Analysis of the Atherosclerosis Risk in Communities Study. Diabetes Care. 2018 Aug 1;41(8):1646–53.
28. Vistisen D, Andersen GS, Hulman A, Persson F, Rossing P, Jørgensen ME. Progressive Decline in Estimated Glomerular Filtration Rate in Patients With Diabetes After Moderate Loss in Kidney Function—Even Without Albuminuria. Diabetes Care. 2019 Oct 1;42(10):1886–94.
29. Stevens LA, Coresh J, Greene T, Levey AS. Assessing Kidney Function — Measured and Estimated Glomerular Filtration Rate. N Engl J Med. 2006 Jun 8;354(23):2473–83.
30. Samra M, Abcar AC. False Estimates of Elevated Creatinine. Perm J. 2012;16(2):51–2.
31. Meyerhardt JA, Kroenke CH, Prado CM, Kwan ML, Castillo A, Weltzien E, et al. Association of Weight Change after Colorectal Cancer Diagnosis and Outcomes in the Kaiser Permanente Northern California Population. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 2017;26(1):30–7.
32. Pappenheimer JR. Paracellular intestinal absorption of glucose, creatinine, and mannitol in normal animals: relation to body size. Am J Physiol. 1990 Aug;259(2 Pt 1):G290-299.
33. Hatakeyama S, Koie T, Narita T, Hosogoe S, Yamamoto H, Tobisawa Y, et al. Renal Function Outcomes and Risk Factors for Risk Factors for Stage 3B Chronic Kidney Disease after Urinary Diversion in Patients with Muscle Invasive Bladder Cancer. PLOS ONE. 2016 Feb 22;11(2):e0149544.

Tables

Table 1. General characteristics.

Variable	Median (Range)
Age (years)	68.3 (28.2 – 86.3)
Weight (Kg)	74 (42 – 135)
Height (cm)	170 (146 – 189)
BMI (kg/m^2)	25.2 (15.1 – 51.4)
Time to death (years)	4.6 (0.5 – 22.1)
Time to dialysis (years)	3.3 (0.03 – 17.4)
eGFR pre surgery ($ml/min/1.73m^2$)	65.8 (5.3 – 132.4)
eGFR at 2 years ($ml/min/1.73m^2$)	58.2 (5.1 – 117.8)
Sex (male) %	73.7
Comorbidities %	
Diabetes	14.7
Hypertension	44.2
IHD	29.3
CVA	9.0
PVD	18.5
Smoker %	
Current	30
Ex smoker	43.9
Chemotherapy %	23.5
Indication for surgery %	
Bladder cancer	93.3
Other	6.7
Surgical technique %	
Wallace	29.8
Bricker	64
Other	6.2
Pathology stage %	
T≥2	75.1
N≥1	47.6
M=1	28

BMI body mass index, eGFR estimated Glomerular filtration rate, IHD ischaemic heart disease, CVA cerebro vascular accident, PVD peripheral vascular disease.

Table 02. Analysis of risk factors for mortality and ESKD.

Variables	ESKD	sig	Mortality	sig
	OR (CI 95%)	p	OR (CI 95%)	p
Age (years)	1.64 (1.02-1.12)	0.01	0.94 (0.92-0.97)	0.001
BMI (kg/m^2)	0.90 (0.79-1.03)	0.11	1.04 (0.97-1.12)	0.30
eGFR pre-operative	1.02 (1.00-1.10)	0.07	0.99 (0.98-1.00)	0.27
Sex (Male/Female)	4.9 (0.6-38.2)	0.09	2.0 (1.2-3.5)	0.01
Diabetes	1.8 (0.5-6.9)	0.38	1.7 (0.8-3.6)	0.19
Hypertension	2.1 (0.7-6.6)	0.20	1.3 (0.8-2.3)	0.26
IHD	1.5 (0.5-4.9)	0.46	1.7 (0.9-3.0)	0.08
CVA	0.8 (0.1-6.7)	0.86	1.0 (0.4-2.4)	1.00
PVD	0.3 (0.1-2.7)	0.30	1.1 (0.5-2.0)	0.87
Smoke	3.8 (0.5-30.1)	0.30	1.6 (0.9-2.9)	0.14
Indication (cancer)	1.4 (0.2-11.5)	1.00	10.1 (3.4-30.2)	0.001
Chemotherapy	2.1 (0.7-6.8)	0.19	1.2 (0.6-2.2)	0.57
Surgical Technique	0.9 (0.9-1.0)	1.00	0.8 (0.4-1.9)	0.65
TNM T≥2	3.4 (1.2-10.3)	0.05	2.3 (1.3-4.2)	0.007
TNM N≥1	2.2 (0.6-8.7)	0.34	1.1 (0.6-1.9)	0.79
TMN M=1	0.6 (0.1-2.8)	0.69	0.7 (0.3-1.4)	0.30

BMI body mass index, eGFR estimated Glomerular filtration rate, IHD ischaemic heart disease, CVA cerebro vascular accident, PVD peripheral vascular disease. The ESKD (end stage kidney disease) group had a significant proportion of patients who are older and stage T≥2. The mortality was associated with age, male gender and RC indication for cancer.

Table 03. Logistic regression analysis for ESKD risk factors.

Variable	p	OR	CI95% LL	CI95% UL
Age (years)	0.001	1.13	1.05	1.22
eGFR pre-operative ml/min/1.73m^2	0.008	1.04	1.01	1.07
Sex (male)	0.09	12.5	0.64	243.5
Tumour T≥2	0.11	3.70	0.76	18.0

* Risk factors associated with ESKD: Age and pre-operative eGFR estimated glomerular filtration rate. OR odds ratio.

Table 04. Logistic regression analysis for mortality risk factors.

Variable	p	OR	CI95% LL	CI95% UL
Sex (male)	0.04	14.8	1.1	192.5
Age (years)	0.002	1.11	1.04	1.18
eGFR pre-operative ml/min/1.73m^2	0.01	1.03	1.01	1.06

* Risk factors associated with mortality: Sex, Age, pre-operative eGFR estimated glomerular filtration rate. OR odds ratio

Figures

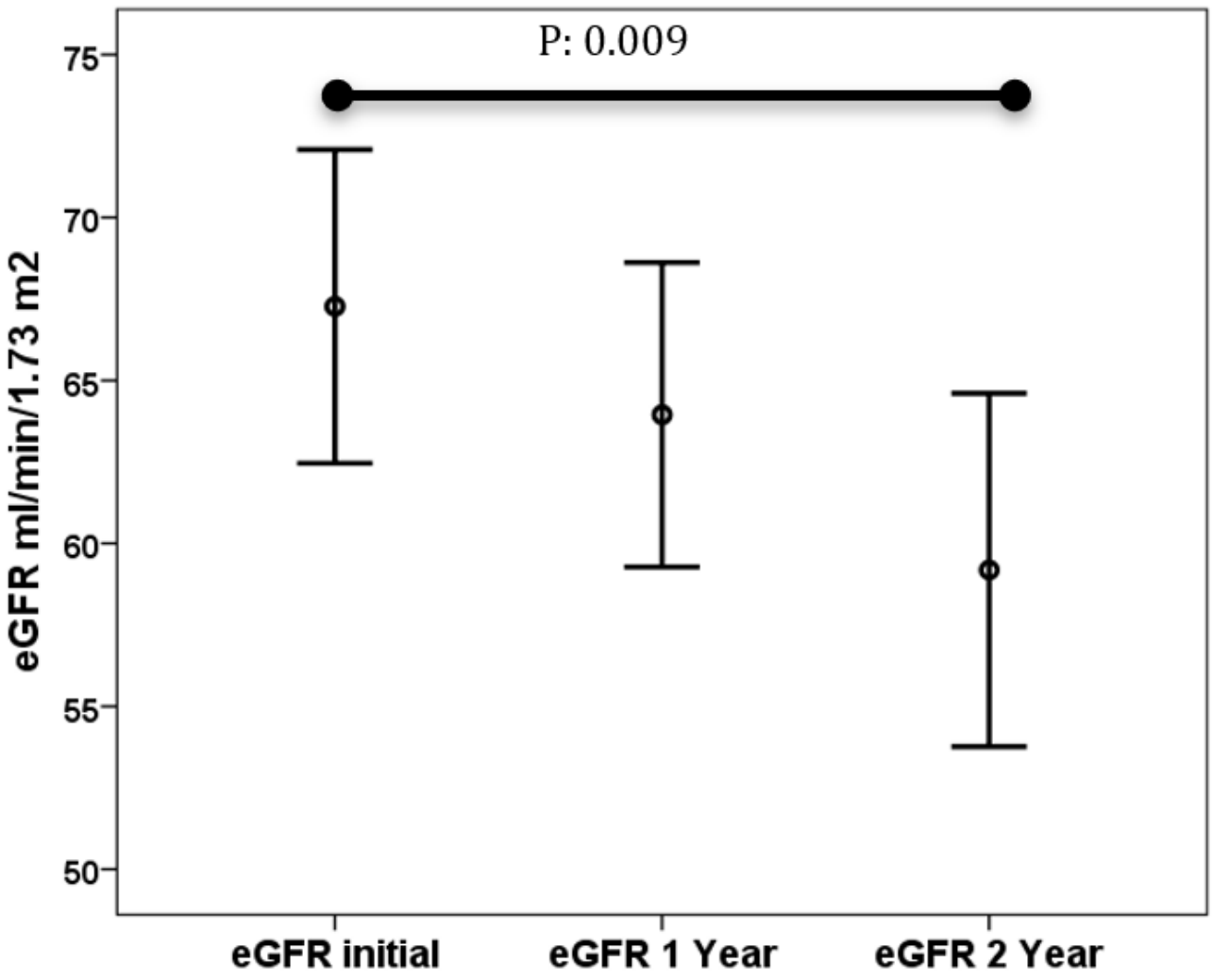

Figure 1

Kidney function change after two years. Change in estimated glomerular filtration rate (eGFR) in patients with radical cystectomy (RC) after 1 and 2 years after surgery.

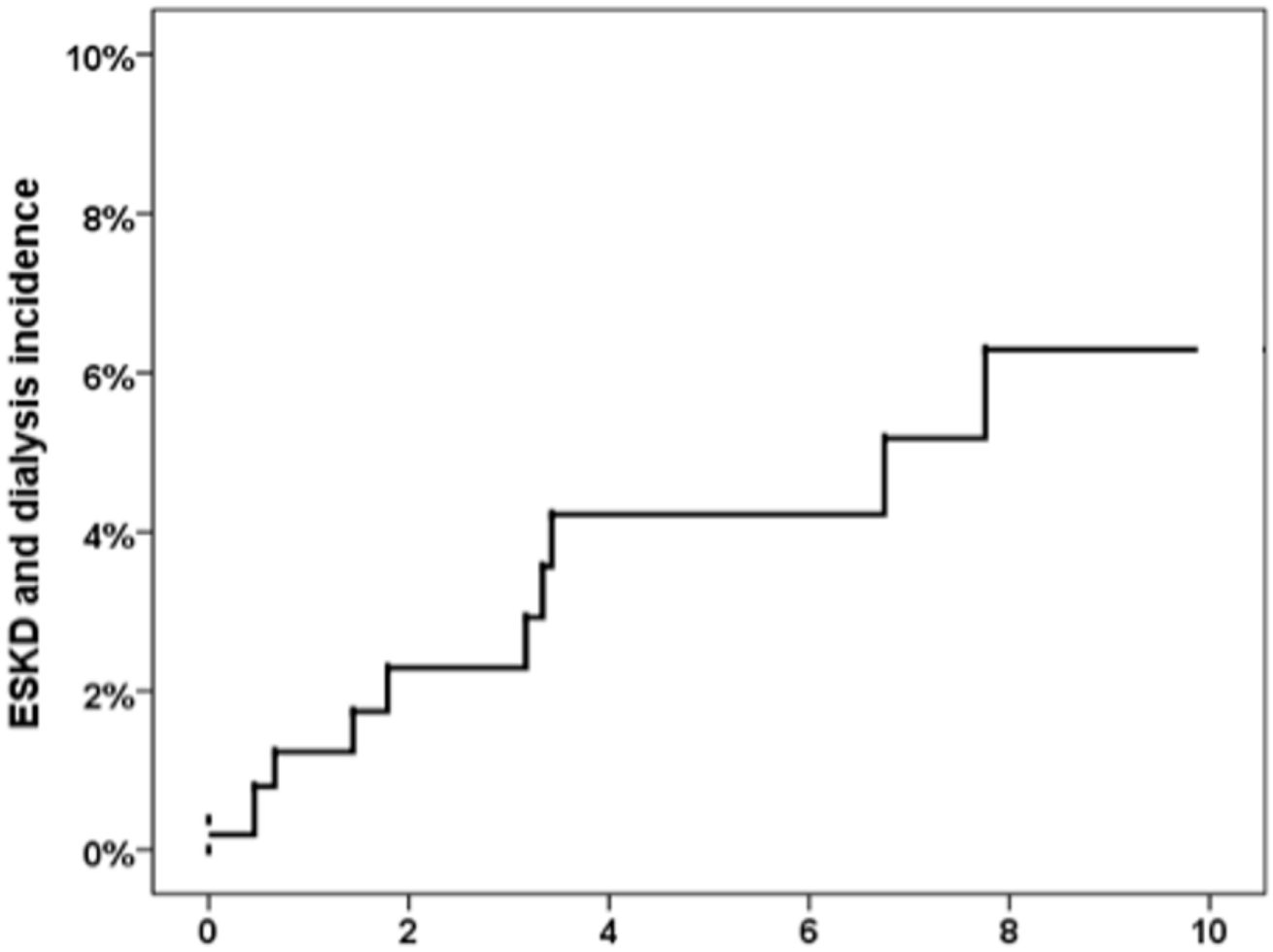

Figure 2

Cumulative percentage of ESKD incidence. Kaplan Meier graphic showing the cumulative incidence of ESKD (end stage kidney disease) 10 years after radical cystectomy.