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Letter to the editor

How to assess renal function in patients with a neobladder

To the Editor

Radical cystectomy and intestinal urinary diversion are standard treatments for patients with localized muscle-invasive bladder cancer. Although long-term survival is increasing, a decline of renal function after urinary diversion is a well-known complication, with a prevalence of 20–70% [1]. The reasons are multiple: ureteral obstruction, pyelonephritis, reflux and factors not specific to urinary diversion (medication, chemotherapy, hypertension, diabetes mellitus). At this moment, there is a paucity of renal outcome data. In addition, a universal definition of how to assess renal function and what can be considered as the optimal diagnostic method is absent [1,2].

As mentioned in a systematic review evaluating renal function in patients undergoing orthotopic bladder substitution, none of the described equations to determine the glomerular filtration rate (GFR) has been validated in this patient group [2]. Historically, inulin clearance is considered as the gold-standard method for measuring GFR. However, this procedure has several disadvantages: (1) it requires a continuous intravenous infusion and multiple, timed urine collections; (2) inulin is not easily available as a ready-to-inject solution for human use; (3) the method is expensive, cumbersome and difficult to perform, due to possible endogenous interferences. A single-injection of radiolabeled [e.g., 51-labeled ethylenediaminetetraacetic acid (^{51}Cr-EDTA) and ^{99m}technetium diethylenetetraminepentaacetic acid (^{99m}Tc-DTPA)] and non-isotopic (e.g. iohexol and iothalamate) tracers has been proposed as an alternative tool for GFR measurement [3,4]. Even if these methods are useful to determine renal function, a small amount of a substance must be injected and several blood samples have to be performed. For these reasons, creatinine-based estimated equations are currently used for diagnosing chronic kidney disease, including Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. However in patients with an orthotopic bladder substitution, a poor correlation has been observed between estimated GFR (eGFR) and ^{51}Cr-EDTA GFR [3]. This is probably due to the resorptive function of the neobladder [5]. Factors that may affect creatinine absorption include the segment of bowel used, its surface area, mucus production, diuresis, duration of urine retention and urinary creatinine concentrations [5,6]. As demonstrated in animal models, reabsorption of urea and creatinine is more active in ileal mucosa, which is used to construct the neobladder, as compared to sigmoid mucosa [7]. On the other hand, exposing ileal mucosa to urine reduces its absorptive capacity [6]. Multiple studies have described the evolution of the mucosa in the neobladder during long term follow-up with a decrease in absorptive capacity. This process of mucosal adaptation reaches a stable situation after one year [8–10]. Finally, low creatinine concentrations have been detected in ileal conduit due to creatinase, leading to an underestimation of GFR [11].

Recent evidence has suggested that cystatin C may be a valuable marker for determining GFR in patients with an orthotopic urinary diversion. In healthy subjects, the urinary concentration of cystatin C is low because cystatin C is absorbed and degraded by the proximal tubules. Therefore, the serum concentration of cystatin C can hardly be affected even if urinary cystatin C is absorbed by the mucosa of the neobladder [12].

In conclusion, interpretation of creatinine-based eGFR should be carried out with caution in patients with a neobladder. Although data are still scanty, cystatin C seems to be a practical and relatively affordable surrogate marker for isotopic GFR in these patients.

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