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CLINICAL EXPERIENCE

Serum cystatin C can be used as a marker of renal function even in patients with intestinal urinary diversion



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Abstract *Objective:* Recently, serum cystatin C (CysC) has been used as a novel marker of renal function. However, there is a lack of data on CysC levels in patients with intestinal urinary diversion (UD). Here we report CysC levels in such patients.

Methods: We prospectively observed 38 patients who were diagnosed with bladder cancer and subsequently treated with radical cystectomy and UD at our institution in 2012 and 2013. Serum creatinine (sCr) and CysC were obtained optionally at the same time at least 1 month after radical cystectomy and UD.

Results: The median CysC and sCr concentrations were 1.12 mg/L (range 0.75–2.47 mg/L) and 0.99 mg/dL (range 0.61–2.22 mg/dL), respectively. The median estimated concentrations of glomerular filtration rate (GFR) based on CysC (eGFR_{Cys}) and GFR based on creatinine (eGFR_{creat}) were 61.08 mL/min/1.73 m² (range 22.64–99.89 mL/min/1.73 m²) and 58.01 mL/min/1.73 m² (range 23.48–91.82 mL/min/1.73 m²), respectively. CysC had a significant correlation with sCr ($r = 0.8607$, $p < 0.0001$) and eGFR_{creat} ($r = -0.8993$, $p < 0.0001$). eGFR_{Cys} also had a significant correlation with eGFR_{creat} ($r = 0.8104$, $p < 0.0001$).

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Conclusion: The correlation between CysC and sCr was strong and the correlation coefficient was equivalent to that in patients without UD. The results suggest that CysC is not affected by UD and can be used as a marker of renal function similarly to sCr in patients with UD.

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Radical cystectomy and intestinal urinary diversion (UD) such as ileal conduit and ilealneobladder substitution are standard treatments for patients with localized muscle invasive bladder cancer. Some patients can obtain long-term survival postoperatively but deterioration of the renal function should be considered as an important complication in the late period [1].

Although inulin clearance is the gold standard for evaluation of renal function, the procedure is too complicated for routine use in the clinical setting. Therefore, renal function is generally evaluated by serum creatinine (sCr) and the estimated glomerular filtration rate (eGFR) based on sCr. Recently, serum cystatin C (CysC) has been used as a novel marker of renal function [2]. CysC is not affected by the amount of muscle or the diet, unlike sCr. In addition, the calculation of eGFR using CysC provides better accuracy than eGFR based on sCr alone [3].

In patients with UD, substances in the urine can be absorbed by the ileal mucosa exposed to the urine [4], which may affect their concentrations in the serum. To date, there has been a lack of data on CysC levels in patients with UD. Here we report CysC levels in such patients.

This study was a prospective observational study of patients who were diagnosed with bladder cancer and subsequently treated with radical cystectomy and UD at Sapporo Medical University Hospital and its affiliated hospitals between 2012 and 2013. The protocol was approved by the institutional review board (acceptance number 23–132). sCr and CysC were obtained optionally at the same time at least 1 month after radical cystectomy and UD. eGFR based on sCr (eGFR_{creat}) was calculated as follows: $eGFR_{creat} \text{ (mL/min/1.73 m}^2\text{)} = 194 \times Cr^{-1.094}$

$\times age^{-0.287}$ (in females: $\times 0.739$) [5]. eGFR based on CysC (eGFR_{cys}) was calculated as follows: $eGFR_{cys} \text{ (mL/min/1.73 m}^2\text{)} = (104 \times CysC^{-1.019} \times 0.996^{age}) - 8$ (in females: $(104 \times CysC^{-1.019} \times 0.996^{age} \times 0.929) - 8$) [6]. Spearman's rank correlation analysis was performed between sCr, sCysC, and eGFR_{creat} as well as eGFR_{cys} and eGFR_{creat}.

Totally, 38 patients consisting of 33 males and five females were enrolled in this study. Their median age was 71 years (range 50–84 years). Of them, 33 (86.8%) and five (13.2%) had an ileal conduit and ilealneobladder, respectively. The median CysC and median sCr concentrations were 1.12 mg/L (range 0.75–2.47 mg/L) and 0.99 mg/dL (range 0.61–2.22 mg/dL), respectively. The median eGFR_{cys} and eGFR_{creat} levels were 61.08 mL/min/1.73 m² (range 22.64–99.89 mL/min/1.73 m²) and 58.01 mL/min/1.73 m² (range 23.48–91.82 mL/min/1.73 m²), respectively. CysC had a significant correlation with sCr ($r = 0.8607$, $p < 0.0001$) and eGFR_{creat} ($r = -0.8993$, $p < 0.0001$) (Fig. 1). eGFR_{cys} also had a significant correlation with eGFR_{creat} ($r = 0.8104$, $p < 0.0001$) (Fig. 2).

To the best of our knowledge, this is the first report measuring CysC in patients with UD. The correlation between CysC and sCr was strong and the correlation coefficient was equivalent to that in patients without UD [7]. The results of this study suggest that CysC can be used as a marker of renal function similarly to sCr and eGFR_{creat} in patients with UD.

In patients with UD, substances in the urine can be reabsorbed by the ileal mucosa exposed to the urine. Rinnab et al. [4] reported that urinary creatinine and urea were potentially reabsorbed into the ilealneobladder, which could affect their concentrations in the serum,

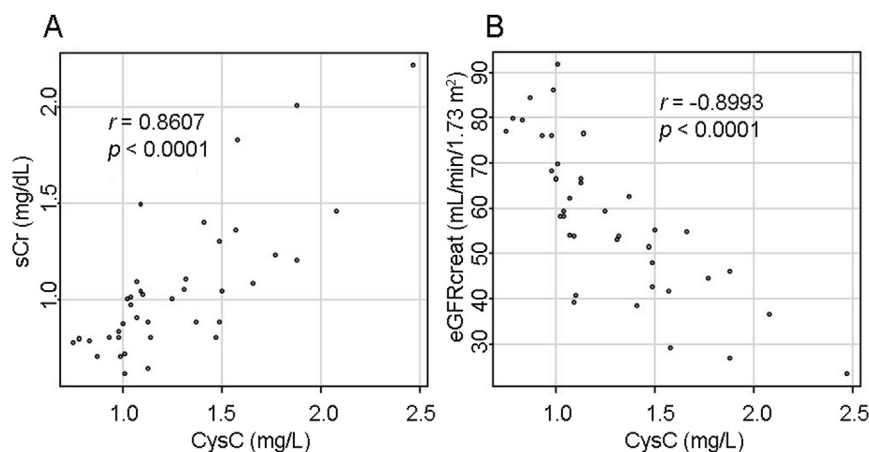


Figure 1 (A) Correlation between CysC and sCr. (B) Correlation between CysC and eGFR_{creat}. CysC, serum cystatin C; sCr, serum creatinine; eGFR_{creat}, estimated glomerular filtration rate based on serum creatinine.

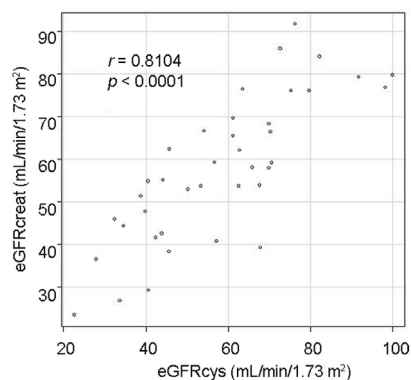


Figure 2 Correlation between eGFRcys and eGFRcreat. eGFRcys, estimated glomerular filtration rate based on serum cystatin C; eGFRcreat, estimated glomerular filtration rate based on serum creatinine.

although the status was different among individuals and the clinical significance was not determined. Cystatin C in the urine can also potentially be absorbed in the ileal segment. However, the urinary concentration of cystatin C in normal subjects is low [8] because cystatin C is absorbed and rapidly degraded by the proximal tubular cells after being filtered in the glomeruli [9]. Therefore, the serum concentration may barely be affected even if urinary cystatin C is absorbed by the ileal mucosa. Essentially, the relationship between CysC and inulin clearance should be verified. However, sCr has been used to assess renal function in patients with UD [1] and the compatibility between CysC and sCr may indicate the clinical usefulness of CysC. Because CysC provides more accuracy in calculation of eGFR, the KDIGO 2012 clinical practice guideline [10] recommend the use of eGFR considering CysC. Therefore we should assess renal function by using CysC to manage chronic kidney disease in patients with UD.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgments

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