Estimated Glomerular Filtration Rate — A More Stable Indicator than Creatinine Clearance in Peritoneal Dialysis Practice

Yoshitaka Maeda, Sayaka Yoshida, Toshiyuki Hirai, Tomoki Kawasaki and Tamaki Kuyama

Nephrology Division, Department of Internal Medicine, JA Toride Medical Center, Japan

Abstract

Objective: The usefulness of estimated glomerular filtration rate may not be restricted to pre-dialysis patients, since we reported that estimated glomerular filtration rate was well correlated with measured total creatinine clearance in peritoneal dialysis patients. To clarify the clinical usefulness of estimated glomerular filtration rate as a parameter for peritoneal dialysis adequacy, we retrospectively surveyed estimated glomerular filtration rate and total creatinine clearance in peritoneal dialysis patients treated at JA Toride Medical Center.

Patients and Methods: A total of 114 data sets of estimated glomerular filtration rate and total creatinine clearance from 21 PD patients treated at JA Toride Medical Center were collected from November 2010 to October 2011. The patients consisted of 15 men and six women with an average age of 66.6 ± 12.6 years (46–95 years old). The average number of samples was 5.4 ± 1.5 (2 to 7) per patient.

Results: The collected data showed less correlation of estimated glomerular filtration rate and total creatinine clearance (r = 0.435) than that of a previous cross-sectional study (r = 0.836). As reported in pre-dialysis patients, the differences between estimated glomerular filtration rate and total creatinine clearance were correlated with total creatinine excretion in urine and PD effluent (r = 0.821). The differences were also correlated with normalized protein catabolic rate, which was one of the main determinant factors for total creatinine excretion (r = 0.636). A similar tendency was apparently observed in one patient with poor compliance to diet therapy and fluctuating dietary intake. From the analysis of these data, serum creatinine seemed to fluctuate less possibly due to compensatory capacity of the residual renal function in small solute clearance.

Conclusions: Consequently, estimated glomerular filtration rate was turned out to be a more stable parameter than total creatinine clearance, which might be a desirable feature in long-term follow-up of peritoneal dialysis patients.

Key words: eGFR, Ccr, PD, creatinine, creatine

Introduction

Weekly creatinine clearance (wCcr) and Kt/V are well-known parameters reflecting dialysis dose and adequacy, and are applied to adjustment of the dialysis menu in each patient who undergoes peritoneal dialysis (PD). However, the limitations of these parameters in predicting survival and morbidity have been reported. Moreover, the collection of urine and peritoneal effluent is cumbersome work not only for patients, but also for medical staff.

Estimated Ccr (eCcr) was proposed as an alternative marker for measured total Ccr (tCcr), because it is less expensive and time-consuming. But it was also reported that eCcr calculated by the Cockcroft-Gault formula substantially overestimated the effect of age on creatinine excretion in PD patients.

Estimated glomerular filtration rate (eGFR) is an alternative marker for measured GFR (mGFR), and it might be a possible indicator for prognosis in the general population without known cardiovascular disease, diabetes or kidney disease and in CKD patients included in the Modification of Diet in Renal Disease (MDRD) study. Moreover, these prognostic features of eGFR might be partially independent of mGFR.

We reported that eGFR was well correlated with tCcr in PD patients by cross-sectional analysis. Similar correlation of eGFR with Ccr was reported by Khosla, et al., although the analyzed patients were restricted to the population with a difference between two measurements of Ccr of less than 25%.

To clarify the actual utility of eGFR in peritoneal dialysis practice, we retrospectively collected the data from 21 PD patients at JA Toride Medical Center for the period of one year.
Patients and Methods

Patients who underwent PD at JA Toride Medical Center for one year or longer were enrolled in the study after their informed consent was obtained. PD patients with a treatment period of less than a year, and patients who underwent combined PD and hemodialysis (HD) therapy were excluded.

To measure renal Ccr, urine was collected for 24 hours (from the second voiding of the day before visiting the hospital to the first voiding on the day of visiting the hospital). PD effluent was also collected for 24 hours on the day before visiting the hospital to measure peritoneal Ccr. The sum of the peritoneal and renal Ccr was defined as the measured tCcr. The serum, urine, and effluent Cr were measured by the established enzyme method.

The formula proposed by the Japanese Society of Nephrology9) was applied for calculation of eGFR as follows:

\[
eGFR \text{ (mL/min/1.73m}^2\text{)} = 194 \times \text{serum Cr}^{-1.094} \times \text{age}^{0.287} \times 0.739 \quad \text{in females}
\]

Protein catabolic rate (PCR) was calculated by the formula proposed by Teehan10) as follows:

\[
\text{PCR (g/day)} = 6.25 \times (\text{urinary urea excretion + peritoneal urea excretion} + 1.39 + 0.15 + 0.031 \times \text{body weight in kg})
\]

PCR was normalized (divided) by the measured body weight (BW) and described as nPCR (g/kg/day).

According to the guidelines of the Japanese Ministry of Health, Labour, and Welfare, informed consent of the patients was obtained. The study protocol was approved by the ethics committee of JA Toride Medical Center.

The data are shown as means ± SD, unless otherwise specified. To observe the correlation of two sets of data, the Pearson’s correlation coefficients were calculated using Excel 2007 (Microsoft, Redmond, WA, U.S.A.).

<table>
<thead>
<tr>
<th>Table 1 Characteristics of the studied patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men / women</strong></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
</tr>
<tr>
<td><strong>CAPD / APD</strong></td>
</tr>
<tr>
<td><strong>Cause of CKD</strong></td>
</tr>
<tr>
<td>DM</td>
</tr>
<tr>
<td>CGN</td>
</tr>
<tr>
<td>NS</td>
</tr>
<tr>
<td>Others</td>
</tr>
<tr>
<td><strong>Treatment period of PD in months</strong></td>
</tr>
<tr>
<td><strong>Samples in the data analysis</strong></td>
</tr>
</tbody>
</table>

5.4 ± 1.5 (2–7) per patient

Results

As Table 1 shows, 21 patients met the inclusion criteria and were included in this study. The patients comprised 15 men and 6 women with an average age of 66.6 ± 12.6 years (46–95 years old), and their average PD period was 45.1 ± 32.4 months (14–118 months). Their causes of CKD were diabetes mellitus (DM) in seven patients, chronic glomerulonephritis (CGN) in seven patients, nephrosclerosis (NS) in four patients, and others in three patients. Continuous ambulatory PD (CAPD) was undertaken in 13 patients, and the other eight patients received automated PD (APD). During the period of one year from November 2010 to October 2011, 114 data sets of eGFR and tCcr from the 21 patients were suitable for data analysis. According to the analysis, eGFR and tCcr were correlated (r = 0.435 in Figure 1). However, their correlation was less than that of a previous cross-sectional study (r = 0.836)7). Unexpectedly lower eGFR levels were observed in one patient (shown as open circles in Figure 1). Repeated counseling of the patient revealed that his diet fluctuated. As Figure 2 shows, tCcr - eGFR difference and total Cr excretion were actually correlated with nPCR in this patient. Similar correlations were observed for the difference between eGFR and tCcr with total Cr excretion.
(r. = 0.821 in Figure 3) and nPCR (r. = 0.636 in Figure 4) in all the data. Total Cr excretion and nPCR were also correlated with each other (r. = 0.516 in Figure 5).

Discussion

This retrospective study with the data collected for a year from 21 PD patients showed that the correlation of eGFR with tCcr was less than that of a previous cross-sec-

Figure 2  tCcr - eGFR difference and nPCR (A) and total Cr excretion and nPCR (B) in one patient who showed fluctuating diet intake. More detailed data from the patient, exhibited as open circles in Figure 1 are shown. Variations in the difference between eGFR and tCcr were correlated with both total Cr excretion and nPCR.

Figure 3  tCcr - eGFR difference and total Cr excretion. Differences between eGFR and tCr were well correlated with total Cr excretion in total samples.

Figure 4  tCcr - eGFR and nPCR. Differences between eGFR and tCcr were correlated with nPCR in total samples.
The difference between tCcr and eGFR was mostly dependent on total Cr excretion, as reported in predialysis patients\(^{11}\), but this has never been reported in PD patients. Moreover, total Cr excretion fluctuated according to the nPCR. Consequently, protein intake estimated by nPCR may affect the difference between tCcr and eGFR.

Because creatinine is homogeneously distributed in the body water, serum creatinine level is determined by the balance of several factors, such as oral intake, generation in the muscle, intrinsic degradation (metabolic clearance) and clearance by peritoneal dialysis and the kidney (Figure 6). The amount of creatinine obtained by oral intake is mainly dependent on the amount of meat, which generally contains 400–460 mg of creatine and creatinine per 100 g, or more precisely, 1 mg of creatinine and 23 mg of creatine per 1 g of meat protein\(^{12}\). Actually, total Cr excretion was well correlated with nPCR in this study (Figure 5). Meanwhile, the Cr generation rate in the muscle is relatively stable, because it is thought to be related to the muscle mass and activity. The metabolic clearance of creatinine is estimated to be between 0.036–0.04 L/kg/day in PD patients\(^{9}\). Thus fluctuating oral intake mainly affects the variance in urinary creatinine excretion, especially in the case of preserved residual renal function, which has a wider ranging capacity for compensation. Consequently, the serum Cr concentration and its calculation product, eGFR, are supposed to be more stable parameters than Ccr by diminishing the preserved capacity in small solutes clearance of the kidney. The increased difference between tCcr and eGFR in the higher PCR population could be explained by a similar reason, because PCR was positively correlated with total Cr excretion. Hence, serum Cr and its calculation product, eGFR, may be superior to Ccr because they are less dependent on diet, unlike Ccr.

Recently, it has been reported that eGFR had a prognostic value for CKD-related complications\(^ {13, 14}\), kidney failure\(^ {6}\), cardiovascular risk factors\(^ {5}\) and mortality\(^ {6}\). It is possible that eGFR has a similar independency and distinct feature as a predictive indicator even in PD patients.

Usually, mGFR is obtained by a single measurement. Hence, the obtained value can fluctuate as a result of several factors, such as patient condition, diet and drugs, which means that mGFR should not always be considered a representative value or “gold standard” of renal function\(^ {15}\), or rather the preserved capacity of the kidney to maintain the serum level of creatinine within a certain range under conditions of fluctuating intake may be a more reasonable index for actual kidney function. Although the peritoneal clearance of small solutes represented by creatinine should be taken into consideration in PD patients\(^ {5}\), eGFR derived from serum creatinine, age and gender may diminish the compensatory fluctuation of small solute clearance in the kidney, and provide a more stable level in each PD patient. This feature may be valuable in routine clinical practice, and it is worth investigating the significance of eGFR as a possible prognostic factor in PD patients, as reported in predialysis patients\(^ {5, 6, 13, 14}\).

This study has some limitations. Because the study design was a retrospective analysis at a single center, the patient characteristics were divergent with respect to PD modalities, exposure periods, residual renal function and adherence to diet therapy. In addition, the study population was small, and equal amounts of data were not collected for each patient. Therefore, differences between individual patients and the entire study population could not be distinguished from the obtained data. However, fluctuating Cr excretion was certainly observed not only in data from individual patient but in all collected data, as shown in Figures 2–5.
Conclusion

This study revealed the practical profile of eGFR, distinct from tCcr, as a more stable marker for small solutes clearance by dialysis and the kidney. A more extended and longitudinal study will be needed to verify the actual value of eGFR in PD practice.

References