Proteinuria/Creatininuria Index and its Correlation With the 24-Hour Proteinuria in Renal Transplanted Patients


ABSTRACT

Background. Proteinuria (P) is a early sign of inflammation and renal damage. It has an important role in the detection, diagnosis, and monitoring of renal disease in transplanted patients. The aim of this study was to examine the correlation between random urinary proteinuria/creatininuria index (P/CI) and 24-hour total protein excretion among stable renal transplant patients.

Materials and Methods. We obtained 1511 samples of 24-hour protein excretion (24-hr P) with corresponding P/CI were obtained from 197 adult patients beyond 6 months post-transplantation between 2009 and 2011. The population was divided into 2 groups: One to obtain a population of justification (755) and another, of validation (755). A scatter graft yielded was obtained by Pearson’s coefficient of correlation. A “receiver operator characteristic curve” analysis was carried out to evaluate the sensitivity and specifity of PCI and 24hr-P, showing a cutoff of 0.15 for PCI.

Results. The PCI and 24 hr P Pearson’s correlation was significant ($r = 0.89; P = .0001$). The sensitivities of the P/CI for the justification and the validation samples were 97% and 94%, respectively; the a cutoff was 0.15. Their negative predictive values for P/CI were 92% and 84% respectively (cutoff, 0.15). The specificity was below 50% in both groups.

Conclusions. We observed a significant correlation between P/CI and 24 hr P. The sensitivity was slightly higher than the specificity (50%) but the negative predictive value was >92%. The use of P/CI seemed to be adequate for screening of protein excretion during renal transplant recipient follow-up.

TOTAL URINE PROTEIN is recognized to be an independent risk factor for cardiovascular and renal disease and as a predictor of end-stage of allograft damage among renal transplant recipients. The recent Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend periodic screening for proteinuria. The amount of protein excretion in the urine has diagnostic and prognostic importance in the initial detection and confirmation of renal disease. Quantification of proteinuria can be of considerable value to assess the effectiveness of therapy and disease progression. Traditionally collection of a 24-hour urine sample is the most commonly accepted way to quantify proteinuria and albuminuria. This is cumbersome for patients to complete, and thus shows poor compliance. Because of protein excretion is reasonably constant throughout the day when glomerular filtration rate is stable, some studies have proposed to use the urine protein/creatinine ratio (PCR) as an alternative method. This simple and convenient method obviates the need for a 24-hour urine collection as well as accurately reflecting changes in the rate of protein excretion.

Studies in nontransplanted patients have evaluated the performance of the urinary albumin-creatinine ratio (ACR) or PCR to predict 24-hr albumin or protein excretion. The
Disease (MDRD) estimated filtration.

transplant number, creatinine, and Modification of Diet in Renal Patients were characterized by gender, age, immunosuppressant, techniques, the differences between the results were plotted against 24-hr P. To assess the concordance between the 2 measurement techniques, the differences between the results were plotted against the average of the 2 methods, as described by Bland-Altman plots.

The population was divided into 2 groups: One to obtain a justification (755) and another for validation (755). A scatter graft was used to obtain the Pearson coefficient correlation. A receiver operating characteristic (ROC) curve was performed to evaluate the sensitivity and specificity of the P/CI and its correlation with 24-hr P. To assess the concordance between the 2 measurement techniques, the differences between the results were plotted against the average of the 2 methods, as described by Bland-Altman plots.

### MATERIALS AND METHODS

We analyzed retrospectively patients with functioning kidney transplantsations followed in a single center between 2009 and 2011. They each provided three 24-hr urine collections together with a concomitant random urine specimen to allow calculation of the PCR.

Patients were all adults (>18 years) showing stable courses beyond 6 months post-kidney transplantation. Stability was defined as the lack of an acute rejection episode or acute kidney injury, which was defined as a (30%) increase in creatinine within a 3-month period. The samples were promptly analyzed by the hospital laboratory using an autoanalyzer (Beckman Coulter DXC800, Fullerton, Calif).

Patients were excluded from the study for the following reasons: (1) Pregnancy or breastfeeding, (2) acute rejection episode within the preceding 3 months and (3) double organ transplantation, for example, kidney and pancreas. We evaluated 197 adult renal transplanted patients. Each participant was instructed in detail on appropriate collection of the 24-hr urine specimen (n = 1511). Patients were characterized by gender, age, immunosuppressant, transplant number, creatinine, and Modification of Diet in Renal Disease (MDRD) estimated filtration.

### Statistical Analysis

The population was divided into 2 groups: One to obtain a justification (755) and another for validation (755). A scatter graft was used to obtain the Pearson coefficient correlation. A receiver operating characteristic (ROC) curve was performed to evaluate the sensitivity and specificity of the P/CI and its correlation with 24-hr P. To assess the concordance between the 2 measurement techniques, the differences between the results were plotted against the average of the 2 methods, as described by Bland-Altman plots.

### RESULTS

The 197 patients provided 1511 24-hr protein excretion samples and corresponding P/CI for the analysis. Age, gender, donor source, time since transplantation included 105 women (53%) and 92 (47%) men of overall mean age of 45.19 year (range, 18–78). The time after transplantation was 1671 (±1035) days. There were 123 cadaveric and 74 living-related transplantations. All patient were prescribed steroids, tacrolimus, and mycophenolic acid for baseline immunosuppression.

Results for urinary creatinine excretion rate, urinary protein excretion, protein creatinin urinary index, serum creatinine and MDRD (ml/m) estimated filtration are also shown in Table 1. The PCI and the 24 hr-P Pearson correlation was significant (r = 0.89; P = .0001; Fig 1). The sensitivity of the P/CI for justification and validation samples were 97% and 94% respectively with a cutoff of 0.15. The negative predictive values were 92% and 84% respectively for P/CI (cutoff 0.15). The specificity was the <50% in both groups (Fig 2A, B).

The ROC curves showed cutoffs of 0.15, that is, the cutoff points recommended by optimal guidelines. The Bland-Altman graph revealed that the differences within a mean ± 1.96 SD were not clinically important; the two methods can be used interchangeably (Fig 3).

### DISCUSSION

The amount of protein excretion in the urine is a widely accepted tool to diagnose and prognosticate the risk to develop renal disease. It is recommended for periodic screening of proteinuria. In renal transplant patients proteinuria is considered to be a surrogate marker of chronic allograft nephropathy and an independent risk factor for cardiovascular disease, the principal cause of death with a functioning graft. Measurement of a spot urine protein by

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<th>Table 1. Patient Characteristic</th>
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<td>Age (yrs)</td>
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<tr>
<td>Female/male</td>
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<tr>
<td>Cadaveric transplant/living transplant</td>
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<tr>
<td>Time since transplantation (d)</td>
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<tr>
<td>Spot urine protein (mg/dL)</td>
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<tr>
<td>Urine creatinine (mg/dL)</td>
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<tr>
<td>24-hr protein excretion (g/L)</td>
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<td>Serum creatinine (mg/dL)</td>
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<td>MDRD (ml/m)</td>
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**Abbreviation:** MDRD, Modification of Diet in Renal Disease. Proteinuria defined as >150 mg/dl.

Results are presented as mean values ± standard desviation for normally distributed data as median (range) for non-normally distributed data.
PCR or ACR has become the standard of care in many transplant centers due to its convenience. It has replaced 24-hr urine protein excretion the gold standard method. Although there are only limited data about its use in renal transplant recipients, information in the literature are sufficient to demonstrate a strong correlation between the protein/creatinine ratio in a random urine sample and the 24 hr protein excretion. Most importantly, PCR can be used to exclude the presence of proteinuria. It can serve as an initial screening test to rule in or rule out proteinuria. Rule out test results show an absence of proteinuria requiring no further action. Several investigators have studied the relationship between 24-hr protein excretion and PRC in renal transplant patients. The sensitivity and specificity, indicated high concordance. The higher values observed for sensitivity compared with specificity suggested that the PCR test may be more valuable as a rule out test.

In agreement with the literature, our study in renal transplant patients also demonstrated a significant correlation between 24-hr protein excretion and PCR in a random urine sample using the Pearson method \( r = 0.89, P < 0.001 \). There were higher values for sensitivity (97%) compared with specificity (50%). We observed a stronger correlation at lower protein excretion values. When the level of protein excretion increased, there was more dispersion.

In summary, a spot urine for PCR is a more acceptable method for patients, because it can easily be collected at a clinic visit and is not subject to the same compliance problems as a 24hr collection. The excellent correlation

![Fig 2. Fractional area under the ROC curve is 0.97 for population of justification (A) and 0.94 for that of validation (B).](image-url)

![Fig 3. Bland–Altman graph. Difference between the results of the 2 methods against the average of the 2 methods.](image-url)
between 24-hr protein excretion and PCR, plus the high sensitivity of the test, make PCR an adequate method for screening of proteinuria among renal transplant patients. A supplemental 24 hr protein measurement may be useful to guide clinical decisions, for example, the need for a biopsy.

REFERENCES


