Urine Protein-to-Creatinine Ratio Is a Reliable Measure of Proteinuria in Lupus Nephritis

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ABSTRACT. ***Objective.*** To evaluate the 24-hour urine protein-to-creatinine (U pr:cr) ratio compared to 24-h urine total protein excretion as a measure of proteinuria in patients with lupus nephritis.

Methods. Proteinuria in 8 patients with lupus nephritis treated with cyclophosphamide was monitored by total protein excretion and U pr:cr ratio in 24-h urine collections. A median of 16 measurements per patient were collected over a median of 47 months. Adequacy of the 24-h collection was assessed by comparing total urine creatinine to the predicted creatinine. Collections in which the difference between the predicted 24-h urine creatinine and the measured 24-h urine creatinine was greater than or equal to 20% were defined as inadequate collections.

Results. Timed 24-h urine collections were frequently inadequate (30.2% of total collections were under-collections, while 14.3% were over-collections). We found 87.5% of patients had at least one under-collection whereas 75% had at least one over-collection. Correlations between total protein and U pr:cr ratio for individual patients ranged from 0.87 to 0.99 (mean 0.95). For the entire sample, the correlation ($R^2 = 0.89$) of total urine protein to Upr:cr ratio was excellent. Excluding the 38 under-collections led to improvement in the overall correlation (0.94). Excluding the 18 over-collections led to a correlation of 0.89. Excluding both under-collections and over-collections led to a correlation of 0.94.

Conclusion. In patients with lupus nephritis, the 24-h U pr:cr ratio is highly correlated with the 24-h urine protein excretion when the collections are adequate. The error of the estimate is higher when collections are poor. (J Rheumatol 2004;31:1557–9)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS
LUPUS NEPHRITIS
PROTEINURIA
PROTEIN-TO-CREATININE RATIO

Quantitation of proteinuria by 24-hour urine collection is a cornerstone of monitoring disease activity in patients with lupus nephritis[1-3]. Such collections, however, are often inaccurate due to collection errors[4-6]. According to the National Kidney Foundation KDOQI Guidelines, proteinuria can be accurately assessed by the use of the urine protein-to-creatinine ratio (U pr:cr)[7]. The ratio is determined by dividing the urine protein (mg/dl) by the urine creatinine (mg/dl). The numerical outcome of the ratio is roughly equal to the 24-h protein excretion in g/day per 1.73 m^2 body surface area[8]. The validity and reliability of this method has been validated in diabetic[9] and nondiabetic[10] nephropathy. An additional prospective cross-sectional study was performed in patients with various glomerular diseases to determine the accuracy of predicting 24-h proteinuria from the Upr:cr ratio. A good correlation and precision of agreement were found between the 2 methods across a wide range of urinary protein, regardless of the level of renal function[11]. There is, however, a paucity of data regarding the utility of Upr:cr ratio for a 24-h urine collection in monitoring proteinuria in lupus nephritis[12]. In this preliminary study, our objective was to evaluate the use of the Upr:cr ratio compared to 24-h urine protein excretion within the same 24-h urine collection as a measure of proteinuria in a cohort of patients with lupus nephritis undergoing intravenous cyclophosphamide therapy.

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MATERIALS AND METHODS

Proteinuria in 8 patients with biopsy-proven lupus nephritis treated with cyclophosphamide was monitored by total protein excretion and Upr:cr ratio in 24-h urine collection. There was a broad 24-h protein range from 112 mg/day to 8456 mg/day. A median of 16 (range: 9-22) measurements per patient was collected over a median of 47 months (range: 18-90). The adequacy of the 24-h collection was assessed by comparing the total creatinine in the sample to the predicted creatinine [(22–(age/9)*kg in women and 28–(age/6)*kg in men][8]. Collections in which the difference between the predicted 24-h urine creatinine and the measured 24-h urine creatinine was greater than or equal to 20% was defined as an under-collection [(predicted–measured)/predicted × 100 > 20%]. Likewise, collections in

which the difference between the measured 24-h urine creatinine and the predicted 24-h urine creatinine was greater than or equal to 20% was defined as an over-collection [(measured–predicted)/predicted × 100 > 20%].

RESULTS

Timed 24-h urine collections were frequently inadequate (30.2% were under-collections, 14.3% were over-collections). Seven (87.5%) of 8 patients had at least one under-collection, and 6 (75%) of 8 patients had at least one over-collection. Individual correlations between total protein and Upr:cr ratio ranged from 0.87 to 0.99 (mean 0.95). In the entire data set, the correlation ($R^2 = 0.89$) was excellent (Figure 1). The overall correlation improved after excluding the 38 under-collections (0.94). Excluding the 18 over-collections led to a correlation of 0.89. Excluding both under-collections and over-collections led to a correlation of 0.94 (Figure 2). The total protein underestimated the Upr:cr ratio by at least 20% in 12 (31.6%) of 38 under-collections, compared to 1 (1.1%) of 88 remaining collections ($p < 0.001$). The total urine protein overestimated the Upr:cr ratio by at least 20% in all 18 (100%) of 18 over-collections, compared to 61 (56%) of the 108 remaining collections ($p < 0.001$).

DISCUSSION

As proteinuria is often the key indicator of kidney involvement in lupus and its response to therapy, it is essential that its accurate measurement be achieved. This is the first study in the lupus literature showing the improved accuracy of the 24-h urine protein-to-creatinine ratio over the standard total 24-h urine protein excretion.

Our study found that the 24-h Upr:cr ratio was highly correlated with the 24-h urine protein excretion when urine collection was adequate. Among inadequate urine collections, however, the 24-h urine protein excretion is a less accurate measure of proteinuria and therefore of renal disease activity. Our study suggests that the lack of perfect correlation of Upr:cr ratio and total protein excretion can be partly explained by inadequate collections.

It should be noted that to correctly interpret the ratio it would be necessary to take into account that the relationship between the ratio and the rate of urinary protein excretion is affected by the concomitant rate of creatinine excretion[13]. In a very muscular individual with high creatinine excretion, or in a frail individual with lower creatinine excretion, the Upr:cr ratio should be interpreted in the context of an accurate measurement of total protein within a 24-h urine performed one time as a baseline. The Upr:cr ratio can then be followed as a surrogate measure of urinary protein excretion.

Studies in non-lupus patients have suggested that the protein excretion rate can be estimated on a single voided urine sample protein/creatinine ratio[5,9]. Future studies need to address the reliability of a random spot Upr:cr ratio as a measure of proteinuria in lupus nephritis compared with the 24-h Upr:cr ratio. Until the validity and reliability of the random (spot) Upr:cr ratio are proven in lupus nephritis, our study suggests that the use of the ratio on a 24-h collection provides the most accurate assessment.

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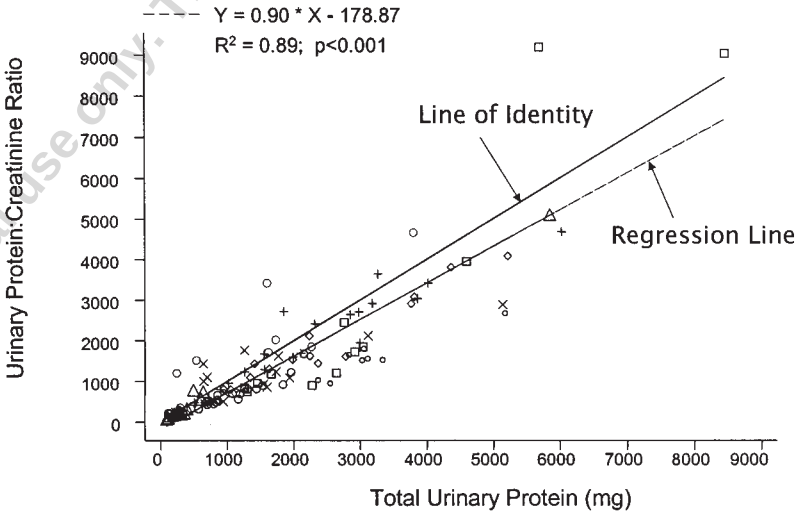

Figure 1. Urinary protein:creatinine ratio versus total urinary protein. Correlations between total protein and Upr:cr ratio for individual patients ranged from 0.87 to 0.99 (mean 0.95). The correlation for the comparison of total urine protein to Upr:cr in the entire sample was $R^2 = 0.89$ (Regression equation $y = 0.90 \times 178.87$).

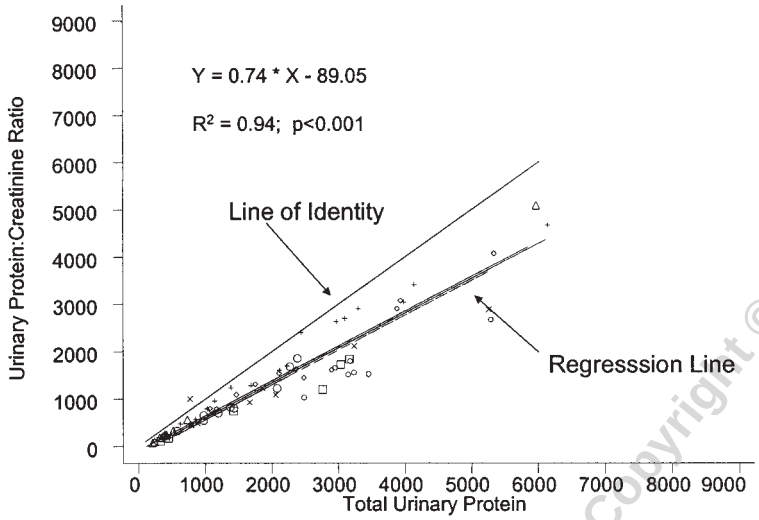

Figure 2. Urine protein:creatinine ratio versus total protein excluding 56 inadequate collections. When the under-collectors and over-collectors are excluded, the correlation between total protein in a 24-hour collection and the Upr:cr improved ($R^2 = 0.94$).

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