Quantitation of Proteinuria by the Use of Protein-to-Creatinine Ratios in Single Urine Samples

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• **Measurements of protein-to-creatinine ratios in single-voided urine samples were compared with 24-hour urinary protein excretions for quantitation of proteinuria in inpatients and outpatients. Patients included those representing a broad spectrum of renal diseases, a wide range of proteinuria, and various degrees of reduction in glomerular filtration rate. Protein-to-creatinine ratios in single-voided urine samples correlated well with measurements of 24-hour urinary protein. This simple single-voided test is reliable and useful in the screening, assessment, and follow-up of proteinuria and avoids the problems associated with 24-hour urine collection.**

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The quantitation of urinary protein excretion is of diagnostic and therapeutic importance to physicians. The degree of proteinuria is indicative of certain types of renal disease and often serves as a useful marker of response to therapy directed at these conditions.[1] The most commonly accepted way of quantitating proteinuria uses the collection of a 24-hour urine sample. This method is cumbersome, inconvenient, and often unreliable, due to the difficulty of accurately collecting a complete 24-hour urine sample. Collections of less than 24 hours in duration are subject to postural and other fluctuations in daily protein excretion.[1,2] The technique of simultaneous determination of urinary protein and creatinine in a single-voided specimen to quantify proteinuria has been evaluated in ambulatory outpatients and found to be reliable.[3] We, therefore, prospectively evaluated single-voided urine specimens for protein-to-creatinine determinations, and compared these with concurrent 24-hour urinary protein excretions in 101 patients. These 101 patients were selected to encompass a wide range of glomerular, interstitial, obstructive, and prerenal conditions, and thus the test group included various degrees of proteinuria and renal impairment. In addition, a combination of hospitalized patients and outpatients were studied to assure the accuracy of this test in immobilized and ambulatory patients.

PATIENTS AND METHODS

One hundred one patients were selected from the patient populations of the Barnes Hospital, St Louis, and the Duke University Medical Center, Durham, NC, to participate in this study. Patients were prospectively selected to provide a wide range of renal function and proteinuria, and a full spectrum of renal diseases (Table). Thirty-three ambulatory outpatients were selected with serum creatinine levels ranging from 0.4 to 9.8 mg/dL (35 to 866 μmol/L), and with 24-hour protein excretion levels ranging from <50 to 9600 mg/24 h (<0.01 to 9.6 g/d). Thirty-f ambulatory inpatients were selected with serum creatinine le ranging from 0.6 to 8.9 mg/dL (53 to 787 μmol/L), and with 24-h urinary protein excretion levels from <50 to 9900 mg/24 h (<0.0 9.9 g/d). Thirty-four immobilized (bed-bound) inpatients were lected with serum creatinine levels ranging from 0.3 to 8.4 mg (27 to 743 μmol/L), and a 24-hour urinary protein determinat ranging from <50 to 8100 mg/24 h (<0.01 to 8.1 g/d). Forty-n patients were women aged 17 to 78 years. Fifty-two patients w men aged 19 to 73 years. Estimated glomerular filtration rate normal in 33 patients (serum creatinine levels less than 1.5 mg. [<133 μmol/L]), moderately impaired in 38 (serum creatin levels, 1.5 to 4.5 mg/dL [133 to 398 μmol/L]), or severely impaire 30 (serum creatinine levels greater than 4.5 mg/dL [>398 μmol/ Body weight varied from 42 to 115 kg. Each subgroup include spectrum of prerenal, glomerular, and interstitial renal disea (Table). Two patients with plasma cell dyscrasias were include the study group.

A random urine sample was obtained from each patient. In cases, the random specimens were obtained during normal wak hours and were never first-morning void samples. First-morn void and evening urine spot samples were avoided because t have been shown to correlate less well with 24-hour prot excretion in normal active outpatients.[3] In ambulatory patier the specimen was obtained after routine upright activity. A ser creatinine determination was obtained on the same day. Imme ately following the collection of the single-voided specimen, a hour urine collection was obtained for protein determinati Serum and urinary creatinine levels were determined by the us an automated method (Astra Autoanalyzer, Beckman Instrume Inc, Somerset, NJ).[4] Urine protein levels were determined by use of an automated method (ACA Autoanalyzer, DuPont Inst ments Inc, Wilmington, Del).[5,6]

RESULTS

The Figure shows the protein-to-creatinine ratio of s gle-voided urine samples as a function of the amount

Renal Disease	No.	Patient Population: Ambulatory Outpatients	Patient Population: Inpatients	Patient Population: Bed-Bound Patients
Diabetes mellitus	10	3	3	4
Glomerulonephritis	20	6	7	8
Hypertension	11	5	3	2
Interstitial nephritis	15	5	8	4
Multiple myeloma	2	0	1	1
Normal	14	9	5	0
Obstructive uropathy	4	1	2	1
Pigment injury	4	0	1	3
Polycystic kidney disease	7	3	2	2
Prerenal or ischemic	9	0	3	6
Vasculitis	5	1	1	3
Total	101	33	34	34

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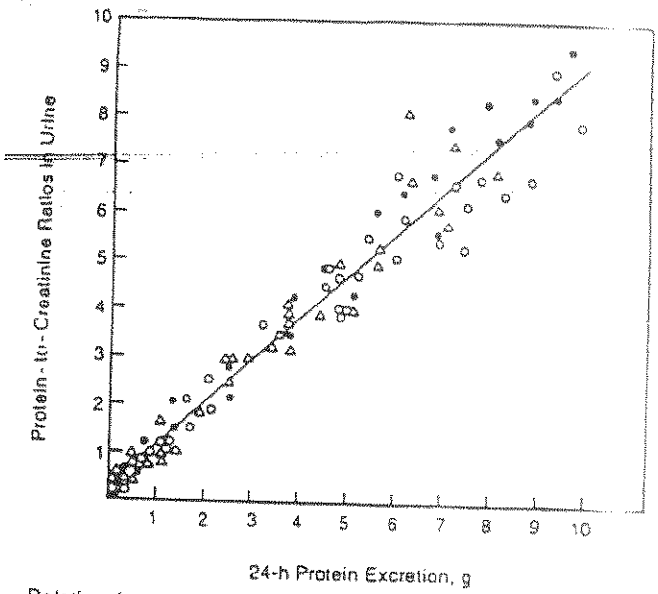

Relation between urinary protein-to-creatinine ratios in single-voided urine specimens and concurrent 24-hour urine protein excretion in ambulatory outpatients (solid circles), ambulatory inpatients (open circles), and immobilized (bed-bound) inpatients (open triangles); $n = 101$; $r = .96$; $y = 0.87x + 0.33$.

protein found in the 24-hour urine collection. The correlation coefficient (least squares method) was found to be significant in all three groups. The correlation coefficient ($r = .96$) is derived from a summary of all three patient populations and is illustrated by the represented line ($y = 0.87x + 0.33$) in the Figure. The correlation coefficient for ambulatory inpatients was $r = .96$ ($y = 0.78x + 0.32$). The correlation coefficient for ambulatory outpatients was $r = .97$ ($y = 0.94x + 0.07$). The correlation coefficient for immobilized patients was $r = .95$ ($y = 0.93x + 0.20$). It can be seen that all patients who excreted more than 3.0 g of protein in 24 hours had protein-to-creatinine ratios that exceeded 3.0. In addition, all patients who excreted less than 200 mg of protein in 24 hours had protein-to-creatinine ratios that were less than 0.2.

COMMENT

The precise quantitation of proteinuria is important in clinical medicine both for the accurate diagnosis of certain diseases and in the follow-up of response to therapy of these conditions. The 24-hour timed urinary collection remains the standard method for quantitation of proteinuria; however, 24-hour timed urinary collections are inconvenient to obtain and frequently unreliable due to inaccurate volume collection. The need for a simple reliable screening test to quantitate proteinuria is readily apparent.

Ginsberg et al,[3] using a limited patient population not classified by type of renal disease, reported success in quantitating proteinuria in ambulatory outpatients by using a ratio of protein-to-creatinine in a single-voided urine specimen. They reasoned that since the glomerular filtration rate is fairly constant in a given patient, a simple ratio comparing protein to creatinine excretion in single-voided samples would accurately reflect quantitative proteinuria, since the two ratios would cancel out the time factor. The study by Ginsberg et al confirmed that proteinuria varied with posture and was most notably decreased at night, associated with recumbency. When single-voided urine samples were collected during normal waking hours and first-morning voided samples were excluded, a high correlation was obtained between 24-hour urinary protein excretions expressed as grams of protein in 24 hours per square meter of surface area and protein-to-creatinine ratios in single-voided specimens. Other investigators, using similar techniques, have found correlations in pediatric populations and in adults with systemic lupus erythematosus.[7,8]

This study represents a prospective comparison of protein-to-creatinine ratios in single-voided specimens with 24-hour urine protein collections in the assessment of proteinuria. This clinical trial significantly expands previous observations by the inclusion of ambulatory and immobilized (bed-bound) patients, and by the prospective selection of a diverse patient population (Table). Patients were selected to include a wide range of renal disease, renal function, protein excretion, age, sex, and body size (Table). All measurements were performed using commonly available autoanalyzers without mathematical adjustments for body surface area. The findings of this study (Figure) indicate a strong correlation for ambulatory outpatients ($r = .97$), ambulatory inpatients ($r = .96$), and immobilized patients ($r = .95$) when random urine samples were obtained during waking hours and first-morning voided specimens were excluded. Further, there were no specific disease groups, levels of renal dysfunction, or degrees of proteinuria for which the test was inaccurate or unsuitable. The urine protein-to-creatinine ratio reliably corresponded with 24-hour urinary collection in men and women independent of renal function, age, or body size. Protein-to-creatinine ratios greater than 3.0 reliably predicted nephrotic proteinuria, while ratios less than 0.2 reflected insignificant protein excretion.

We conclude that determining the ratio of protein-to-creatinine in single-voided urine samples is an accurate, convenient, inexpensive, and reliable estimate of total proteinuria in the vast majority of patients. This simple test remains accurate independent of the amount of proteinuria, degree of renal dysfunction, or condition causing the proteinuria. We propose that the protein-to-creatinine ratio in single-voided urine samples may be even more reproducible than the 24-hour urinary protein excretion now used as the most common clinical method of quantitating proteinuria.

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