International Journal of Nephrology and Renovascular Disease

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ORIGINAL RESEARCH

Proteinuria: an ignored marker of inflammation and cardiovascular disease in chronic hemodialysis

This article was published in the following Dove Press journal:
International Journal of Nephrology and Renovascular Disease
22 December 2011
Number of times this article has been viewed

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Background: Cardiovascular disease is the leading cause of morbidity and mortality in hemodialysis (HD) patients, the main etiologies being diabetes and hypertension. Cardiac and inflammatory biomarkers are usually employed to assess risk or damage, or during follow-up. Proteinuria is considered a strong predictor of morbidity, a cause of inflammation, oxidative stress, hemodynamic alteration, and progression of chronic kidney disease. However, proteinuria is rarely considered in the clinical assessment of HD patients.

Methods: This was a concurrent, cohort-observational, cross-sectional study in which 52 chronic HD subjects were divided into three groups according to the degree of proteinuria: Group (G) A: <1 g/day, n = 25; GB: 1–3 g/day, n = 13; GC: >3 g/day, n = 14. Baseline hemoglobin, albuminemia, cholesterol, body mass index, Malnutrition-Inflammatory Score, pro-B-type natriuretic peptide, troponin T, C-reactive protein (CRP), and ultrafiltration rates were analyzed.

Results: There was no difference between groups in terms of baseline age, gender, hypertension, cause of renal failure, hemoglobin, cholesterol, albumin, CRP levels, cardiac biomarkers, adiponectin, body mass index, or Malnutrition-Inflammatory Score. Time on HD: GA, 34.56 ± 23.3 (range [r]: 6–88); GB, 25.15 ± 19.40 (r: 6–58); GC, 18.21 ± 9.58 (r: 6–74) months; $P = 0.048$. Proteinuria: GA, 0.33 ± 0.30 (r: 0.0–0.88); GB, 1.66 ± 0.54 (r: 1.03–2.75); GC, 7.18 ± 2.80 (r: 3.04–21.5) g/day; $P < 0.001$. Mean ultrafiltration rates were significantly different: GA, 2.80 ± 0.73; GB: 1.85 ± 0.96 liters/session; $P = 0.003$. Fourteen diabetic patients were identified (27%): GA, 3 (12%); GB, 3 (23%); GC, 8 (57%); $P = 0.009$. A positive and significant correlation was observed between diabetes and proteinuria >3 g/day: rho 0.438, $P = 0.027$. Although troponin T, pro-B-type natriuretic peptide, adiponectin, and CRP were not different among groups, the positive correlation between troponin T and CRP elevated significantly as proteinuria increased: GA, rho 377, $P = 0.063$; GB, rho 663, $P = 0.013$; GC, rho 687, $P = 0.007$.

Conclusion: In chronic HD, nephrotic-range proteinuria was significantly higher in diabetic nephropathy patients versus other causes. This was associated with inflammation and cardiac stress and was independent of fluid removal. Proteinuria >3 g/day was associated with shorter time on HD. Whether severe proteinuria is associated with shorter survival in HD, independent of diabetes, is to be determined. Proteinuria should be considered in the assessment of cardiovascular and inflammatory states in HD patients.

Keywords: hemodialysis, proteinuria, inflammation, cardiovascular risk

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Introduction

Patients with end-stage renal disease are at high risk of developing cardiovascular disease. Other mechanisms that interplay with cardiovascular factors increasing

morbidity and mortality in individuals with chronic kidney disease (CKD) are, among others, protein-energy wasting, malnutrition, inflammation, and the interrelationships between these that may emerge. There are several clinical, nutritional, and biochemical parameters that may be indicative of a chronic inflammatory state in individuals with CKD, particularly those on dialysis.[1] Many risk factors and metabolic alterations observed in the uremic milieu may contribute to the excessive risk of cardiovascular disease. Both the Framingham cardiac risk score[2] and the so-called nontraditional risk factors, such as inflammation, endothelial dysfunction, sympathetic overactivation, protein-energy wasting, oxidative stress, vascular calcification, and volume overload, may play relevant roles in the development of vascular disease in dialysis patients.[2–5] However, Wang et al[6] have recently demonstrated that the addition of multimarker scores (including markers of inflammation and volume overload) to conventional risk factors resulted only in small increases in the ability to grade risk, at least in the general population.[7]

Proteinuria is another predictor of increased cardiovascular risk in the general population.[8] Numerous studies have shown that treating patients with diabetic/nondiabetic CKD and proteinuria reduces proteinuria and slows progression of renal disease, and that the greater the reduction in proteinuria, the greater the benefit.[9–11] In addition to predicting CKD progression, proteinuria is a well-established risk marker for cardiovascular disease.[12–15] Reduction in proteinuria confers significant reduction in cardiovascular events. The Reduction in End Points in Noninsulin-Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan (RENAAL) study showed that albuminuria is the most important factor in predicting the cardiovascular risk in patients with type 2 diabetic nephropathy and, at 6 months, for every 50% reduction in albuminuria, an 18% reduction in cardiovascular risk and a 27% reduction in heart failure was reported.[16] It is evident that proteinuria has tremendous predictive value in cardiac failure, both as a marker of future events and as a therapeutic target.[9] Patients with diabetic nephropathy and proteinuria >3 g/g have a 2.7-fold higher risk for heart failure when compared with patients with low proteinuria (<1.5 g/g).[16] Moreover, proteinuria has been shown to be the strongest predictor of cardiovascular outcomes, including hospitalization for heart failure.[16] Extinguishing proteinuria by decreasing blood pressure, hyperfiltration states, and sodium intake, as well as tightly controlling glycemia, are generally accepted potential strategies to reduce cardiovascular risk events.[9] Although the nature of the links between proteinuria and vascular disease may be partly due to endothelial dysfunction, persistent low-grade inflammation also plays a role. Indeed, inflammation is associated with both endothelial dysfunction and albuminuria.[17,18]

It is noteworthy, despite this active attempt to reduce proteinuria in predialysis patients to delay disease progression, proteinuria appears to be forgotten or even ignored by nephrologists once a patient enters dialysis. However, its existence may certainly continue conferring the well-known inflammatory, catabolic, thrombotic, and toxic effects on the endothelium that it exerts in the predialysis period.[18–20] In this study, the different degrees of proteinuria in chronic hemodialysis (HD) patients were determined and its association with nutritional, inflammatory, and cardiovascular markers of disease was assessed.

Methods

Design

Concurrent, cohort-observational, cross-sectional study on 52 chronic HD patients.

Patients

The Institutional Review Board of the Hospital Británico de Buenos Aires was notified about the collection of data for the cross-sectional study. Informed consent was obtained from each patient enrolled. Patients aged below 18 or over 85 years, or with a history of neoplasia, acute infection, hepatopathy, nontreated hypothyroidism, anuria, or body mass index >40 kg/m^2 were excluded. No patients with human immunodeficiency virus, hepatitis B virus, or hepatitis C virus were included. No failed transplant patients were included. There was no difference in history of tobacco use among the groups: Group (G) A: 3; GB: 1; GC: 1. Out of 58 patients examined, 52 chronic HD patients who had been treated for more than 3 months were included; six patients were excluded due to anuria: one due to bilateral nephrectomy, two due to polycystic kidney disease, and three due to primary glomerulonephritis.

Patients were divided into three groups according to the degree of proteinuria: GA, proteinuria <1 g/day (n = 25); GB, proteinuria 1–3 g/day (n = 13) and GC, proteinuria >3 g/day (n = 14).

Blood measurements

The following blood measurements were taken for each enrolled patient: C-reactive protein (CRP), hemoglobin, albumin, Malnutrition-Inflammatory Score (MIS), pro-B-type natriuretic peptide (pro-BNP), troponin T,

adiponectin, and mean intradialytic ultrafiltration rate. Nutritional assessment was performed employing the MIS, and this was updated in the authors' center every 3 months while the anthropometric measurements were obtained at the end of a dialysis session at the end of the respective trimester. Hemoglobin, cholesterol, and serum concentrations of albumin were measured by routine procedures. High-sensitivity CRP (normal value: <0.3 mg/dL) was calculated by immunoturbodimetry using a VITROS 5.1® FS Chemistry System (Johnson & Johnson, New Brunswick, NJ). For pro-BNP, a chemoluminiscence method was employed using a VITROS ECi® Immunodiagnostic System (Johnson & Johnson): (normal values: <125 pg/mL for subjects <75 years; <450 pg/mL for subjects >75 years). Troponin T was measured by electrochemoluminiscence, using a Cobas e411 immunology analyzer (Roche Diagnostics, Indianapolis, IN) (normal value: <0.01 ng/mL). Adiponectin was determined by DIAsource ELISA KAPME09 (Linco Corp, Littlerock, CA) (normal values: female, 10.2 ± 4.6 μg/mL; male, 6.8 ± 4.1 μg/mL). Blood was drawn in fasting conditions prior to the HD session. Proteinuria was collected as a 24-hour urine sample; collection started the day before blood would be drawn (ie, the day of the dialysis session). All biochemical measurements were done at the Central Laboratory of the Hospital Británico.

HD aspects

Thrice-weekly HD sessions were performed using biocompatible membranes (Polyflux 10 L®; Gambro, Stockholm, Sweden) and bicarbonate bath and with a mean dialysis blood flow rate of 450 ± 50 mL/minute, and dialysate flow rate of 500 mL/minute and a mean duration per session of 4.0 ± 0.5 hours. The ultrafiltration rate employed in this study was the one registered by the automatic dialysis machines (Surdial 190; Nipro®, Osaka, Japan) when the blood samples were collected. Kt/V and normalized protein catabolic rate (nPCR) were calculated (Table 1).

Arteriovenous accesses

Arteriovenous access was fistulae in 29 patients (56%), polytetrafluoroethylene grafts (Gore-tex® vascular graft; WL Gore and Associates, Inc, Newark, DE) in ten patients

Table 1 General patient data

Patient characteristics	Group A Proteinuria <1 g/day (n = 25)	Group B Proteinuria 1–3 g/day (n = 13)	Group C Proteinuria >3 g/day (n = 14)
Age (years)	68.85 ± 11.85	59.72 ± 19.06	61.48 ± 16.27
Gender			
Males	17 (68%)	8 (61.5%)	11 (78.6%)
Females	8 (32%)	5 (38.5%)	3 (21.4%)
Time on hemodialysis (months)*	34.56 ± 23.3 (r: 6–88)	25.15 ± 19.40 (r: 6–58)	18.21 ± 9.58 (r: 6–74) Diabetics* 16.4 ± 4.5 Nondiabetics* 21.6 ± 2.3
Hypertensives, n = 32 (61.54%)	17 (68%)	7 (53.8%)	8 (57.1%)
Diabetics,** n = 14 (27%)	3 (12%)	3 (23%)	8 (57%)
Urinary output (mL/day)	756 ± 367	688 ± 299	606 ± 382
Proteinuria*** (g/day)	0.33 ± 0.3 (r: 0.0–0.88)	1.66 ± 0.54 (r: 1.03–2.75)	7.18 ± 2.80 (r: 3.04–21.5)
Cholesterol (mg/dL)	179 ± 21	198 ± 37	188 ± 35
Albumin (g/dL)	3.99 ± 0.37	3.94 ± 0.36	3.70 ± 0.56
CRP (mg/dL)	1.44 ± 2.61	0.82 ± 1.07	1.10 ± 1.41
Pro-BNP (pg/mL)	23581 ± 48341	12053 ± 32318	15621 ± 41695
Troponin T (ng/mL)	0.06 ± 0.06	0.03 ± 0.02	0.06 ± 0.06
Adiponectin μg/mL	12.16 ± 7.55	12.99 ± 10.95	13.67 ± 7.29
MIS	4.92 ± 2.33	5.00 ± 1.88	4.79 ± 3.12
Body mass index	27.02 ± 4.16	25.76 ± 4.58	27.73 ± 5.63
Ultrafiltration rates (L/session)	2.08 ± 0.72	1.85 ± 0.5	2.22 ± 1.17
Kt/V	1.33 ± 0.1	1.29 ± 0.1	1.31 ± 0.1
nPCR (g/kg/day)	1.05 ± 0.27	1.11 ± 0.38	1.09 ± 0.49

Notes: *$P < 0.048$; **$P < 0.009$; ***$P < 0.001$.

Abbreviations: MIS, malnutrition-inflammatory score; nPCR, normalized protein catabolic rate; r, range; CRP, C-reactive protein; Pro-BNP, pro-B-type natriuretic peptide.

(19%), tunneled catheters (Tessio® [Medcomp®, Harleysville, PA] or Quinton® Permcath™ [Covidien AG, Mansfield, MA]) in 13 patients (25%). Nonsignificant differences according to access distribution were reported among the three groups.

Hypertension

Patients with blood pressures >140/90 mmHg were considered to be hypertensive.

Cardiovascular disease

Cardiovascular disease was defined as the presence, based on clinical grounds, imaging and laboratory results, of cardiac ischemic disease, and/or peripheral vascular disease and/or cerebrovascular disease at the time of the study.

Medications

Most of the patients were on angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta blockers, aspirin, or other commonly used drugs at stage 5 chronic renal disease (such as calcium salts, potassium chelators, erythropoietin, intravenous L-carnitine, intravenous iron, statins, omeprazole, folic acid, vitamins, and benzodiazepines).

Statistics

Results are expressed as the median (range [r]), unless stated otherwise. Fisher's exact or chi-square tests were employed for categoric variables. For continuous variables, the Mann–Whitney test was used and for intervariable correlations. Spearman's rank and ρ (rho) coefficient were also calculated. *P* values ≤0.05 were considered significant.

Results

Patients were not different according to baseline mean age (years): GA: 68.85 ± 11.85; GB: 59.72 ± 19.06; GC: 61.48 ± 16.28; *P* = nonsignificant. Gender; hypertension; cause of renal failure; hemoglobin; cholesterol; albumin; CRP levels; cardiac biomarkers troponin T, pro-BNP, and adiponectin; MIS; Kt/V; nPCR; and ultrafiltration rates were included (Table 1). Time on HD: GA, 34.56 ± 23.3 (r: 6–88) versus GB, 25.15 ± 19.40 (r: 6–58) versus GC, 18.21 ± 9.58 (r: 6–74) months, *P* = 0.048 (Table 1). Proteinuria: GA, 0.33 ± 0.30 (r: 0.0–0.88); GB, 1.66 ± 0.54 (r: 1.03–2.75); GC, 7.18 ± 2.80 (r: 3.04–21.5) g/day, *P* < 0.001. Proteinuria was present in 87% of the dialysis population. When considering all study patients included, only seven (13%) patients from GA did not have proteinuria (all other GA patients had proteinuria, and all patients from GB and GC had proteinuria). No differences were observed with regard to vascular accesses among the three groups. Hypertensive subjects: n = 32, 61.54%; GA: 17 (68%); GB: 7 (53.8%); GC: 8 (57.1%). Fourteen diabetic patients were identified (27%): GA, 3 (12%); GB, 3 (23%); GC, 8 (57%), *P* = 0.009. A positive and significant correlation was observed between diabetes and proteinuria >3 g/day: rho 0.438, *P* = 0.027. Causes of end-stage renal disease in GC are shown in Table 2. In GC, median proteinuria between diabetics (n = 8) versus nondiabetics (n = 6): 6.57 (r: 3.19–21.5) versus 5.36 (r: 3.04–10.7) g/day, *P* = nonsignificant. Although troponin T, pro-BNP, and CRP were not different among groups, the positive correlation between troponin T and CRP elevated significantly as proteinuria increased: GA, rho 377, *P* = 0.063; GB, rho 663, *P* = 0.013; GC, rho 687, *P* = 0.007.

Discussion

In CKD patients, proteinuria is a common event, irrespective of cause, and virtually all patients with CKD present with varying degrees of proteinuria.[21] However, in dialysis patients, the prevalence of proteinuria is unknown. In the present study, proteinuria was present in 87% of the hemodialyzed population. It is noteworthy that, despite significant differences in proteinuria among the three groups, these changes were not accompanied by significant alterations in albuminemia or cholesterolemia. This phenomenon could be attributed to the similar nutritional status the three groups displayed and to the use of statins in virtually all patients. In patients with proteinuria >3 g/day, the two main causes of end-stage renal disease were diabetes nephropathy and primary glomerulonephritis, although no

Table 2 Group C characteristics

Variable	Group C Proteinuria >3 g/day, n = 14
Diabetes mellitus	8
Glomerulonephritis	5
Polycystic kidney disease	1
Overall proteinuria (g/day) mean ± SD	7.18 ± 2.80
Proteinuria in diabetics, n = 8 (g/day)	6.57 (r: 3.19–21.5)
Proteinuria in nondiabetics, n = 6 (g/day)	5.36 (r: 3.04–10.7)
Arteriovenous fistula	5
Arteriovenous grafts	3
Catheters	6
CRP (mg/dL), median	0.45 (r: 0.1–4.6)
Pro-BNP (pg/mL), median	1475.0 (r: 149–15,800)
Troponin T (ng/mL), median	0.032 (r: 0.01–0.22)
Adiponectin (μg/mL), median	14.36 (r: 3.49–24.48)
MIS, median	3.50 (r: 2–11)
Body mass index, median	28.15 (r: 20.1–41.3)
Ultrafiltration rates, median (L/session)	2.4 (r: 0.5–4)

Abbreviations: SD, standard deviation; CRP, C-reactive protein; MIS, malnutrition-inflammatory score; Pro-BNP, pro-B-type natriuretic peptide.

significant differences in the amount of proteinuria between diabetics and subjects with glomerulonephritis were observed between both subpopulations. However, there was a significant increase in diabetic patients in GC in comparison to the other two groups, and a relative increase in the diabetic population was observed as proteinuria augmented. Proteinuric levels did not correlate with body mass index or the type of vascular access, and could not be attributed to hypertension or to hemodynamic fluctuations, as pro-BNP measurements were not different among the groups. There was a significant difference in the ultrafiltration rates between GA and GB, but this could not be associated to any of the variables under consideration, particularly with pro-BNP or adiponectin, between which important feedback regulations exist. Interestingly, as shown in Table 3, as proteinuria worsened, a significant correlation developed between troponin T, a cardiovascular biomarker, and CRP, an inflammatory marker. This interrelationship may suggest that proteinuria could interact covertly and be an ignored culprit in the complex and chronic protein-energy wasting syndrome dialysis patients live in, contributing to a higher risk of cardiovascular disease and inflammation as proteinuria worsens.

In one of our local databases belonging to CKD patients recruited in year 2010, proteinuria was present in 204 subjects (76.98%). Interestingly, proteinuria significantly worsened as kidney function declined and the highest rates of proteinuria were encountered in the most advanced stages of the cohort: Stage 3, 1.39 ± 3.2 g/day (r: 0.0–21.6) in 80% of the 90 cases included versus Stage 4, 1.87 ± 0.99 g/day (r: 0.0–5.1), which represented 95% of the 37 individuals included in this group. At Stage 5D, proteinuria was present in 85% of the 60 patients included and the mean level of proteinuria was 2.48 ± 3.72 g/day (r: 0.0–21.5). This level of proteinuria was significantly higher and different from Stages 3 ($P = 0.001$) and 4 ($P = 0.013$). These findings underscore previous findings that demonstrated that proteinuria is associated with CKD, worsens renal function, and is highly prevalent in end-stage renal disease.[9–11,21]

Cardiovascular disease is the main cause of death in the CKD population. However, cardiovascular disease can be the final pathophysiological pathway where many different entities may converge: Framingham factors, malnutrition, oxidative stress, calcium-phosphate metabolism, anemia, infections, and inflammation. Although many of the traditional Framingham risk factors have been included in this study, only diabetes mellitus was significantly more frequent in GC compared with the other groups (Table1). In CKD, the main causes that lead to renal replacement therapies are diabetic nephropathy, hypertension, and glomerulonephritis. In all these entities, cardiovascular disease is a major cause of morbidity and mortality, and proteinuria again plays a key role in these pathophysiological processes. In this study, higher degrees of proteinuria (>3 g/day) significantly correlated with troponin T and CRP, markers of cardiovascular stress and systemic inflammation (Table 3).

The question is, therefore, what the relationship among CRP, troponin T, and proteinuria in HD is, if indeed there is such a relationship. Both CRP and troponin T have been employed as markers of highly prevalent complications as inflammation and cardiovascular disease in dialysis subjects. CRP has been reported to be elevated in 30%–60% of dialysis patients and can be employed as a predictor of cardiovascular mortality in HD.[22] In addition, it has been established that troponin T levels are increased in subjects with renal failure, even in the absence of myocardial ischemia.[23,24] In fact, approximately 53% of patients with CKD present with elevated troponin T without acute myocardial necrosis.[25] As troponin T is normally cleared by the kidneys, it could be elevated in CKD owing to delayed clearance.[26] However, other reasons could also explain the high troponin T levels, such as left ventricular hypertrophy, congestive heart failure, and sepsis.[24,25,27] The combination of increased levels of CRP and troponin T levels is associated with an increased risk of death in CKD.[28] Wong et al state that the positive correlation between troponin T and CRP could be due to an inflammatory process that could induce a subclinical myocardial damage resulting from endothelial injury and atherosclerosis.[29] How does proteinuria fit into this process? In dialysis, proteinuria could be an important cause of inflammation, endothelial dysfunction, atherosclerosis, and peripheral vascular disease as in previous stages of CKD,[11,30] triggering CRP and troponin T elevations. This situation could mean that as proteinuria worsens, the correlation found between troponin T and CRP increases significantly (Table 3).

Therefore, it ought to be reasonable to target proteinuria for treatment, as its decrease may result in better residual kidney function and cardiovascular status in Stage 5D subjects. However, once patients are started on dialysis,

Table 3 Correlations between troponin T and C-reactive protein in the different groups

	Group A	Group B	Group C
	C-reactive protein	C-reactive protein	C-reactive protein
Troponin T	ρ = 0.377 *P* = 0.063	ρ = 0.663 *P* = 0.013	ρ = 0.687 *P* = 0.007

Note: ρ, Spearman coefficient.

proteinuria is generally ignored as a potential factor of morbidity and mortality; but proteinuria may contribute to the burden of cardiovascular disease and should be paid attention to in dialysis patients. Therefore, despite patients with proteinuria being on dialysis, the condition should be controlled as its persistence may hasten the loss of residual renal function, a relevant item to preserve at any price in this population.

Moreover, proteinuria is not only important as a marker of progression of renal disease but is also associated with catabolic processes, protein-energy wasting, hypoalbuminemia, and inflammation. All these processes are prevalent in the dialysis community.[1,7] However, the data relating proteinuria and HD are more than scant. In a work published by Goldwasser and Kaldas in 1999, in which they observed a rise in albumin and creatinine in those patients who entered dialysis after 6 months of treatment, they hypothesized that this phenomenon could be attributed, in part, to a better nutritional status, gain in muscle mass, and to a decline in residual renal function.[21] This decrease in urinary output could consequently result in lower losses of protein in the urine. It is well-known that as proteinuria progresses and, more importantly, when there is no medical intervention focused specifically on it, parenchymal fibrosis ensues and residual renal function rapidly deteriorates.

One question that needs to be addressed for dialysis patients is the threshold above which proteinuria could be implicated in inflammatory processes and contribute to the development of cardiovascular disease. Should the levels of proteinuria be interpreted in the same way as in predialysis subjects? This study suggests that as proteinuria increases, cardiovascular stress and inflammatory processes are more likely to be encountered. No data exists on whether proteinuria should be treated in dialysis or, in that case, the level of treatment to pursue. The authors' data suggest that proteinuria should be treated, considering its association with inflammation and cardiovascular stress. Although, as mentioned above, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers could have modified these results, the drugs were employed homogeneously in the three groups.

Finally, this study has found that as proteinuria worsens, there is a trend to shorten time on HD (Table 1). Whether this is due to a higher proportion of diabetic patients, who have a lower survival rate than nondiabetics, or to higher degrees of proteinuria, cannot be concluded from the present study. However, the authors underscore the critical importance proteinuria may play in HD as a forgotten, overlooked marker of cardiovascular disease and inflammation.

This study has many limitations. Due to the small number of cases included, conclusions must be drawn cautiously. In this respect, in GC the significant correlation found between CRP and troponin T may be associated with heavy proteinuria, but other factors not assessed in this study may also be involved. Other inflammatory molecules, such as interleukin 6 and tumor necrosis factor or endothelial and procoagulant molecules like plasminogen activator inhibitor-1, were unable to be measured. These molecules are more accurate as markers of inflammation than CRP and would have certainly added more information to the data presented in this study. Further, no vascular arteriosclerotic parameters such as pulse wave velocity were evaluated in the patients in this study, which would have certainly enriched the primary findings. Moreover, as an observational study of a cross-sectional cohort, no follow-up with regard to patient prognosis, the evolution of proteinuria and its correlation with other biomarkers, or mortality rates could be obtained. All these results require validation. However, the authors believe this work will be a call to attention for nephrologists regarding another important aspect of the characteristics of urinary output and residual renal function in dialysis patients.

Conclusion

In chronic HD, diabetes was significantly associated with obesity. Nephrotic range proteinuria was significantly higher in diabetic nephropathy patients versus other causes and was associated with inflammation and cardiac stress. Proteinuria should be considered in the assessment of cardiovascular and inflammatory states of HD patients. Diabetes was associated with shorter time spent on HD. Whether severe proteinuria is associated with shorter survival in HD, independent of diabetes, is yet to be determined.

Disclosure

The authors declare no conflicts of interest in this work.

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