Clinical and laboratory variables associated with quality of life in Brazilian haemodialysis patients: a single-centre study

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Background: Amongst chronic diseases, end-stage renal disease (ESRD) deserves special attention in the context of health-related quality of life (HRQOL). ESRD affects quality of life more intensely than heart failure, diabetes, chronic lung disease, arthritis and cancer. In addition, patients who perceive low HRQOL withdraw from dialysis treatment more commonly. **Aim:** To identify clinical and laboratory variables associated with health-related quality of life (HRQOL) in hemodialysis (HD) patients. **Patients and methods:** We included 174 chronic HD patients from a single unit aged 18 years and older who never received a kidney allograft and survived the first three months of treatment. We used the Khan index to assess comorbidity and the Medical Outcomes Study 36-Item Short Form Health Survey Questionnaire (SF-36) to measure HRQOL. **Results:** Amongst the eight domains of HRQOL, physical role had the lowest score (35.0 ± 43.0) and social function the highest (64.3 ± 27.7). In the multivariate analysis, age was associated with seven of eight domains, excepting bodily pain. Albumin was associated with five of eight domains. Time on dialysis, hemoglobin and calcium-phosphorus product were associated with physical function, bodily pain and vitality, respectively. **Conclusions:** Age and albumin were the main variables associated with quality of life, and the calcium-phosphorus product was associated with a strategic domain: vitality. Attention to albumin and ageing effects, control of the calcium-phosphorus product and improvement of physical conditioning are necessary to achieve better HRQOL (Rev Méd Chile 2008; 136: 1264-71).

(Key words: Calcium-phosphorus; Hemodiafiltration; Quality of life; Serum albumin)

Variables clínicas y de laboratorio asociadas a la calidad de vida de pacientes brasileños en hemodiálisis. Estudio de un centro

Antecedentes: La enfermedad renal terminal afecta la calidad de vida relacionada a salud más que la insuficiencia cardíaca, la diabetes, enfermedad pulmonar crónica y cáncer. Los pacientes que tienen una baja calidad de vida, se retiran de los tratamientos dialíticos con más frecuencia. **Objetivo:** Identificar variables clínicas y de laboratorio asociadas a la calidad de vida relacionada a salud, en pacientes en hemodiálisis crónica. **Pacientes y método:** Se estudiaron 174 pacientes en hemodiálisis crónica, mayores de 18 años y que nunca hubieran recibido un trasplante renal. Se utilizó el índice de Khan para evaluar comorbilidades y el cuestionario SF-36 (36-Item Short Form Health Survey Questionnaire) para evaluar calidad de vida relacionada a salud. **Resultados:** De los ocho dominios que comprende el cuestionario, el rol físico obtuvo el puntaje más bajo (35.0 ± 43.0) y la función social, el más alto (64.3 ± 27.7). En el análisis multivariado, la edad estaba asociada con siete de los ocho dominios, exceptuando dolor corporal. La albúmina estaba asociada con cinco de los ocho dominios. El tiempo en diálisis, la hemoglobina y el producto calcio-fósforo se asociaron con función física, dolor corporal y vitalidad, respectivamente. **Conclusiones:** La edad y albúmina fueron las variables más asociadas a calidad de vida. El producto calcio-fósforo se asoció a vitalidad, un dominio estratégico. Para mejorar la calidad de vida, se debe prestar atención a la albúmina y los efectos del envejecimiento, se debe controlar el producto calcio-fósforo y mejorar la condición física.

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Traditionally, clinical variables are used in medical practice to tailor interventions and determine prognosis concerning organ dysfunction and death. In chronic disease states, another outcome must be put in perspective, since medical technology can postpone death and minimize some organic complications, but throughout the lifetime the morbid condition affects many dimensions of patients' daily activities. In fact, quality of life is perceived by patients as being an important outcome in the scenario of chronic diseases.

Health-related (HRQOL) is associated with the various aspects of life that are affected by a person's health status¹. During the 1990s there was a large increase in medical research about HRQOL². Nowadays HRQOL, along with efficacy and security, is a primary outcome in many clinical trials. There are some well-validated instruments to measure HRQOL in patients as well as the general population. However, the high cost involved in validating such instruments inhibits creation of new instruments. SF-36 is being widely used in medical research and to measure population life quality parameters in many countries.

Amongst chronic diseases, end-stage renal disease (ESRD) deserves special attention in the context of HRQOL. ESRD affects quality of life more intensely than heart failure, diabetes, chronic lung disease, arthritis and cancer³. In addition, patients who perceive low HRQOL withdraw from dialysis treatment more frequently⁴. Perhaps no other marker can indicate this risk. Indeed, withdrawal is responsible for one-fourth of deaths in haemodialysis (HD) patients⁵. Unfortunately, kidney transplants, which offer the best life quality, are not accessible to many patients because of the worldwide shortage of organs^{6,7}. Hence, reliable associations of objective variables, such as from clinical or laboratory studies, are useful for health professionals involved in caring for HD patients.

Due to the multifactorial profile of HRQOL, it is not surprising that researchers find a multiplicity of associations, especially in multicentric studies with large samples⁸. Since 2004 we have been focusing on HRQOL regarding a small sample from a single renal unit, the only one in the northern region of Ceará state in northeast Brazil. The clinical characteristics of this sample, however, are similar to those in other underdeveloped

areas: young patients with low-comorbidity. There is a great deal of research from developing countries about HRQOL in older, high-comorbidity and diabetic patients, but ESRD can affect patients of any age. Nephrologists all over the world, particularly in South America, care for poor patients with clinical characteristics of our sample and need more data about them. Thus, we aimed to identify what clinical and laboratory variables are independently associated with HRQOL in HD patients at a single dialysis unit in northeast Brazil.

PATIENTS AND METHODS

Sample. The study was performed at the Dialysis Unit of Santa Casa Hospital, in Sobral, Ceará, Brazil. From March 2004 to March 2006, we included consecutive ESRD patients older than 18 years of age undergoing haemodialysis for at least three months, who had not received transplants. Amongst 139 patients on HD in March 2004, 108 were included. The reasons for leaving the others out were: 16 with less than three months on haemodialysis, 4 had previously received transplants, 7 patients refused and 4 were under 18 years of age. Until the end of the study in March 2006, a further 56 patients were included. During the study period, the only reason for exclusion was the death of 29 patients before three months on haemodialysis. Thus, there were 164 participants in the study. All patients were submitted to conventional HD (three times a week) with polysulfone dialysers (maximum number of reuse =12). The study protocol and informed consent were approved by the ethics committee of the Federal University of Ceará.

Measurement of quality of life. We used the validated Brazilian version of the Medical Outcomes Study 36-Item Short Form Health Survey Questionnaire (SF-36) to measure the HRQOL level⁹. This is a well-validated 36-item questionnaire covering issues relating to physical, psychological and social functioning that generates scores from 0 (worst) to 100 (best) concerning 8 domains: physical function (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social function (SF), role-emotional (RE) and mental health (MH). PF scores patients'

performance related to daily activities, RP regards the impact of physical health on life, BP evaluates pain level and its impact on normal daily activities, GH evaluates subjective perception about present and future health status and resistance to illness, VT scores patients' feelings about their energy, vitality and moments of fatigue, SF scores the impact of health on routine social activities, RE measures the influences of emotional status on daily activities, and MH scores humour and well-being, including depression and anxiety. Two nurses were trained in the use and purpose of the SF-36. The SF-36 was administered by the nurses and one author.

Patient data. The demographic data, time on dialysis and underlying aetiology of ESRD were assessed via unit records. Underlying kidney disease was classified by clinical criteria and not by histopathology. Educational level was graded as: 1 - up to 4 years of schooling; 2 - more than 4 years. Every patient was assigned a low, medium or high risk index based on comorbidity, as described by Khan et al¹⁰. Khan's comorbidity index takes into consideration age in three classes and nine comorbidities: diabetes, myocardial infarction, angina pectoris, congestive heart failure, liver cirrhosis, obstructive pulmonary disease, systemic collagen disease, pulmonary fibrosis and visceral malignancies. The laboratory results are those routinely measured in haemodialysis patients and correspond to the mean of three months, including the month when SF-36 was administered and the months before and after its administration. Creatinine, haemoglobin, albumin, calcium and phosphorus were measured with standard methods by the same laboratory throughout the study. KtV (dialysis dose index) was estimated using a second-generation Daugirdas formula¹¹, and like other laboratory results, is presented as a three-month average.

Statistical analyses. Continuous and category variables are presented as mean $\pm$ SD and percentages, respectively. Scores related to the eight domains of HRQOL were generated by a specific SF-36 programme. For univariate analysis, we calculated the Pearson correlation coefficient of age, time on dialysis and laboratory results with scores generated by the SF-36. We used the

Spearman coefficient to estimate the correlation between comorbidity and HRQOL scores. For multivariate analysis, we employed stepwise linear regression including the following clinical and laboratory variables: sex, age, time on dialysis, comorbidity, creatinine, haemoglobin, albumin, calcium-phosphorus product and KtV. Statistical significance was considered to be a P value of <0.05 . All the statistical analyses were carried out using the SPSS version 13.0 package programme.

RESULTS

The mean age of the sample was 43 ± 15 years (range 18-83), 64.6% were male, and mean time on dialysis was 39 ± 44 months (median =19.0; range 3-191). The most prevalent primary kidney diseases were glomerulonephritis (49.4%) and hypertension (26.8%). The complete demographic and laboratory data are shown in Table 1.

Amongst the eight domains related to quality of life, role-physical presented the lowest score (35.0 ± 43.0) and social function the highest (64.3 ± 27.7), as shown in Table 2.

In the univariate analysis, all eight variables studied were correlated with at least one HRQOL domain. However, age (except for bodily pain) and albumin (except for role-emotional) were correlated with seven of eight domains. The correlations were negative for age and positive for albuminemia. The correlation coefficients are shown in Table 3 and 4. Comorbidity was associated with physical function, role-physical and role-emotional (Table 5).

In the multivariate analysis, only age and albumin were associated with various life-quality domains. Nonetheless, time on dialysis, haemoglobin and calcium-phosphorus product were each associated with a specific domain, respectively, physical function, bodily pain and vitality, as shown in Table 6.

DISCUSSION

Our sample is very singular: there were few diabetics, so young patients with predominance of glomerulonephritis as the primary kidney disease made up the majority, with a small number of

Table 1. Patient data

Clinical and laboratory variables		
Sex		
	Male	106 (64.6)
	Female	58 (35.4)
Age		43±15
Race		
	White	66 (40.2)
	Mulatto	82 (50.0)
	Black	16 (9.8)
Level of education		
	Grade 1	128 (78.0)
	Grade 2	36 (22.0)
Job		
	No	140 (85.4)
	Yes	24 (14.6)
Income (monthly)		
	≤US\$ 200	119 (72.6)
	>US\$ 200	45 (27.4)
Time on dialysis (months)		39 ± 44 (median =19.0)
Primary kidney disease		
	Glomerulonephritis	81 (49.4)
	Hypertension	44 (26.8)
	Diabetes	12 (7.3)
	Polycystic kidney disease	8 (4.9)
	Chronic pyelonephritis	8 (4.9)
	Lupus	7 (4.3)
	Obstructive uropathy	4 (2.4)
Comorbidity*		
	Low risk	124 (75.6)
	Medium risk	29 (17.7)
	High risk	11 (6.7)
Creatinine (mg/dl)		13.0±3.3
Haemoglobin (g/dl)		10.0±1.9
Albumin (g/dl)		4.3±0.6
Calcium-phosphorus product (mg ² /dl ²)		66.3±23.7
KtV		1.49±0.3

Data are means ± SD, or percentages (in parentheses)

*Khan index

participants with advanced comorbidity. The worldwide pattern is the reverse: diabetes is the principal primary kidney disease, with predominance of elderly and high-risk patients¹².

This is a typical sample of underdeveloped areas of the globe, where infectious diseases are

the main public health problem and medical assistance to patients with chronic diseases are inadequate. Indeed, diabetics in these regions die from cardiac complications before developing ESRD, which appears after many years the onset of diabetes. Brazil has socioeconomic disparities

Table 2. Mean scores related to quality of life

Domains	Score
Physical function	59,0±27,0
Role-physical	35,0±43,0
Bodily pain	59,0±28,0
General health	43,0±22,0
Vitality	52,0±23,0
Social function	64,3±27,7
Role-emotional	43,0±45,0
Mental health	64,0±23,0

and many regions due to its continental size, resulting in different profiles of haemodialysis

patients. But even in larger and richer cities of southeast Brazil - and indeed in many large cities of the world - patients with the profile of ours can be found in poor and peripheral areas.

Despite the underdeveloped profile, our HD patients presented role-physical as the lowest (worst) score and social function and mental health as the highest (best) scores. Role-physical pertains to physical, and social function and mental health to the mental component of HR-QOL. This is in accordance to North American and European results, which show mental aspects less affected than physical ones in HD patients^{3,13,14}. Considering the young age and low-grade comorbidity of our patients, it is serious to find so much impact in the role-physical category. This smaller

Table 3. Pearson correlations between laboratory variables and quality of life

Domains	Laboratory variables									
	Cr		Hb		Alb		CaP		KtV	
	r	P	r	P	r	P	r	P	r	P
PF	0.140	0.080	0.047	0.558	0.301	<0.001	0.036	0.648	-0.219	0.005
RP	0.118	0.140	0.123	0.121	0.176	0.026	0.146	0.066	-0.015	0.846
BP	0.206	0.009	0.209	0.007	0.308	<0.001	-0.004	0.956	-0.076	0.336
GH	-0.044	0.578	0.080	0.313	0.242	0.002	-0.046	0.562	-0.039	0.622
VT	0.059	0.457	0.157	0.047	0.258	0.001	-0.090	0.257	0.010	0.893
SF	0.098	0.218	0.107	0.179	0.276	<0.001	0.199	0.011	-0.055	0.483
RE	0.058	0.470	0.078	0.326	0.129	0.105	0.076	0.340	-0.119	0.136
MH	0.035	0.656	0.119	0.132	0.168	0.034	-0.001	0.987	0.035	0.656

PF: physical function; RP: role-physical; BP: bodily pain; GH: general health; VT: vitality; SF: social function; RE: role-emotional; MH: mental health; Cr: creatinine (mg/dl); Hb: haemoglobin (g/dl); Alb: albumin (g/dl); CaP: calcium-phosphorus product (mg²/dl²).

Table 4. Pearson correlations between age and time on dialysis and quality of life

Domains	Clinical variables			
	Age		Time on dialysis	
	r	P	r	P
Physical function	-0.259	0.001	-0.133	0.104
Role-physical	-0.194	0.017	-0.064	0.432
Bodily pain	-0.152	0.063	-0.109	0.182
General health	-0.200	0.014	-0.155	0.058
Vitality	-0.275	<0.001	-0.029	0.723
Social function	-0.279	<0.001	-0.012	0.884
Role-emotional	-0.213	0.008	0.042	0.609
Mental health	-0.195	0.016	0.028	0.727

Table 5. Spearman correlations between comorbidity and quality of life

Domains	Comorbidity*	
	r	P
Physical function	-0.183	0.019
Role-physical	-0.198	0.011
Bodily pain	-0.107	0.171
General health	-0.130	0.096
Vitality	-0.093	0.232
Social function	-0.109	0.161
Role-emotional	-0.188	0.015
Mental health	-0.041	0.597

*Khan index

Table 6. Stepwise linear regression of clinical and laboratory variables with quality of life

Variables	Domains							
	PF	RP	BP	GH	VT	SF	RE	MH
Age	-	-	-	-	-	-	-	-
	-0.312 [†]	-0.262 [†]		-0.232 [†]	-0.298 [†]	-0.293 [†]	-0.260 [†]	-0.217 [†]
Time on dialysis	-0.187*							
Hb			0.175*					
Alb	0.218 [†]		0.276 [†]	0.268 [†]	0.270 [†]	0.250 [†]		
CaP					-0.207 [†]			

PF: physical function; RP: role-physical; BP: bodily pain; GH: general health; VT: vitality; SF: social function; RE: role-emotional; MH: mental health; Hb: haemoglobin (g/dl); Alb: albumin (g/dl); CaP: calcium-phosphorus product (mg²/dl²)

*p <0.05. [†]p <0.01

role-physical, together with poor social status and treatment restrictions, can be one determinant of the low percentage of patients with a job. Efficient interventions with physical conditioning programmes are reported in the literature^{15,16}. We think that better physical status will lead to more job opportunities amongst patients in such a productive age range.

The quality of treatment evaluated by the laboratory variables can be considered good. The mean laboratory results are adequate to recommended targets for abuminemia and dose of dialysis¹⁷. The mean haemoglobin is 1 g/dl below the target. The calcium-phosphorus product is

over recommended level, reflecting the difficulty in practice to control it adequately.

Age and albumin were the most important correlators with HRQOL. Their correlation was maintained in the multivariate model. Most information about the age effect on HRQOL comes from research on patients older than 65. In these, quality of life is lower than in the general age-matched population^{18,19}. The average age of our sample is far below 65 and we found age negatively associated with both physical and mental aspects, in contrast to various studies where ageing affects more physical than mental components of quality of life^{20,21}.

Albumin is a traditional marker of morbidity and mortality²², and in our study it was positively associated with five of eight HRQOL domains. Its level decreases because of malnutrition or inflammatory activity. Unfortunately, a cross-sectional study design cannot clarify this association: Does low albumin affect HRQOL or low HRQOL interfere with diet, causing low albumin?

Comorbidity was correlated with three domains in the univariate analysis, but contrary to our expectations, not in the multivariate model. Probably this occurred because despite the grade of comorbidity, the consequences expressed by laboratory markers, such albumin, are the most important association. We can establish that HRQOL in our sample can be more affected in patients with low albumin than those patients with comorbidities but without such alteration.

Calcium-phosphorus product, like albumin, is also a strong predictor of morbidity and mortality in HD patients²³. This is derived from the deposition of calcium-phosphorus in soft tissues and also in arteries, affecting coronary and myocardial function, as well as causing ischemia of body segments²⁴. Even though calcium-phosphorus product was associated with only one domain, we considered vitality a strategic domain, and believe this association has to be borne in mind by health providers treating patients with high calcium-phosphorus product. We did not find this association in literature. Recent study reveals hypercalcaemia, but not calcium-phosphorus product, associated with poor mental health²⁵.

It was surprising to us that time on dialysis was only associated with physical function, since time on dialysis is associated with so many medical complications. The median time on dialysis of only 19 months in our sample can be an explanation for the lack of this association.

We intentionally chose medical instead of socioeconomic factors to analyze due to the

homogeneity of poor socioeconomic profile. It seems to us that some clinical variables studied can be modified, unlike the socioeconomic situation of our patients. The results reported here can improve the quality of care by achieving interventions concerning sub-groups at risk of poor outcomes. Control of diet and inflammation by checking albumin was always our concern and needs more attention regarding HRQOL. In the same way, control of calcium-phosphorus product gains importance in the perspective of life quality. Finally, the poor level related to role-physical indicates the need for exercise programmes, which have been shown to be efficient in literature.

There are several limitations to this study. Firstly, the sample size is modest. Secondly, our results may not hold for patients without the singular characteristics as ours. Thirdly, cross-sectional evaluation makes it difficult to draw conclusions regarding causality by correlations and regression analysis. However, despite these limitations, the strength of our research regards its objective, in other words, the fact our analysis involves individual life quality domains helps to determine individual aspects of HRQOL which require priority attention by health care providers of similar patients.

In conclusion, clinical and laboratory variables such as age and albumin were significant and independently correlated with quality of life concerning almost all HRQOL domains assessed by SF-36. Vitality, a very strategic life-quality domain, was also associated with a third variable: the calcium-phosphorus product. Interventions must be planned to control albumin and calcium-phosphorus product, as well as close follow-up of ageing in patients who remain on dialysis without transplantation. Finally, the very low score in role-physical domain in such a youthful sample calls for particularly efficient interventions.

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