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Original Article

The impact of malnutrition in morbidity and mortality in stable haemodialysis patients

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Abstract

Background. When assessed by single biochemical measurements, malnutrition in dialysis patients is associated with increased mortality, but there are few data evaluating abnormalities in anthropometry or composite nutritional scores and outcome. The aim of our study was to ascertain the prevalence and severity of malnutrition in 761 stable patients from 20 haemodialysis centres and its influence in morbidity and mortality after one year of follow-up.

Methods. Malnutrition was estimated by scoring four anthropometric indexes; body mass index (BMI), triceps skinfold thickness (TSF), mid-arm circumference (MAC), and mid-arm muscle circumference (MAMC); three biochemical measurements; serum albumin, serum transferrin and total lymphocyte count; and clinical examination. Mortality and hospitalizations were collected prospectively during the year of follow-up.

Results. A moderate/severe degree of malnutrition was presented by 51.6% of male and 46.3% of female patients. TSF was moderate–severely decreased in 41% without differences between males and females. MAMC was moderately decreased in 19.8% of males and in 8.1% of females ($P<0.001$). Multiple logistic regression analysis showed that the predictors of malnutrition were: age >65 years (OR = 1.96, CI: 1.22–3.14), male sex (OR = 1.95, CI: 1.24–3.07), comorbidity index (OR = 1.23, CI: 1.03–1.45), time on dialysis (OR = 1.13, CI: 1.08–1.18), duration of dialysis (OR = 0.73, CI: 0.63–0.85) and PCR related to ideal body weight (OR = 0.17, CI: 0.06–0.50).

After 1 year of follow-up, data from 442 patients were available. A total of 68 patients died (15.4%) with cardiovascular diseases being the most frequent cause of death (57.3% of the cases). The predictors of mortality were: age (OR = 1.06, CI: 1.03–1.09), cardiovascular disease (OR = 2.13, CI: 1.19–3.83), neurological disease (OR = 2.96, CI: 1.41–6.15), nephroangiosclerosis (OR = 2.34, CI: 1.10–4.98) and total lymphocyte count (OR = 0.93, CI: 0.87–0.98). Hospitalization was needed in 44% of patients. The comorbidity index, serum albumin and age were the predictive factors of hospitalization.

Conclusions. Protein–calorie malnutrition is frequent in haemodialysis patients. Fat depletion predominated in both sexes. Duration of dialysis and protein catabolic rate related to ideal body weight was the only predictor which could be influenced by a nutritional intervention. Morbidity appeared to be influenced by the comorbidity index and age was the strongest predictor of mortality. The only nutritional measurements predictive of morbidity and mortality were serum albumin and total lymphocyte count respectively. Therefore, the influence of malnutrition in morbidity and mortality can not be definitively stated.

Key words: haemodialysis; hospitalization rate; malnutrition; mortality; protein catabolic rate

Introduction

For over 20 years, protein–calorie malnutrition has been reported as a frequent complication in patients on maintenance haemodialysis therapy and it has been attributed to several causes, including inadequate intake of protein and energy, inhibition of protein synthesis and/or stimulation of protein degradation [1–5]. Its prevalence has varied from 25–75% among the series published [6–16]. These differences could be partially explained by the methods used in the assessment of the nutritional status; anthropometric measurements, biochemical determinations or a combination of both. Despite the high prevalence of malnutrition in patients on haemodialysis, no multivariate analysis investigating the factors which predict the development of abnormal anthropometry is available.

The importance of malnutrition is due to the fact that suboptimal nutritional status in haemodialysis

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patients has been associated with an increased morbidity and mortality [11,17–25]. However, in the majority of these studies the evaluation of malnutrition was mainly based on the measurements of serum albumin and other serum proteins and there are a few but no definitive studies where malnutrition mostly evaluated by anthropometric parameters, was associated with increased mortality [12,13]. Furthermore, the possible effects of malnutrition cannot be easily separated from the effects of the underlying disease. Patients on chronic haemodialysis have additional complicating conditions such as cardiovascular, gastrointestinal and liver diseases. These complications can produce anorexia and malnutrition and this could be a marker of illness rather than the cause of death [3].

Among the biochemical parameters, hypoalbuminaemia has been considered to be the single most important predictor of death [20–25]. Low values of serum albumin have been attributed to poor nutritional status, but recently hypoalbuminaemia has been considered to be a non-specific marker of inflammation [26,27]. As in other situations, and in the enthusiasm to promote the importance of nutrition, other significant and perhaps more fundamental factors that predispose haemodialysis patients to death may have been overlooked.

We conducted a multicentre study in our country to try to answer some of these issues. In this study, we have evaluated the prevalence of malnutrition in a group of stable patients on maintenance haemodialysis therapy and the possible risk factors involved in its development. In addition, the role of malnutrition in morbidity and mortality in the haemodialysis patients was investigated. Malnutrition was assessed by a combination of anthropometric and biochemical measurements.

Patients and methods

Patients

A total of 761 patients on haemodialysis from 20 facilities in the central region of Spain (Madrid and surrounding provinces) received a full nutritional evaluation between January and March 1993 and were followed-up for 1 year. Informed consent was obtained in every case. The criteria for inclusion in the study were: (i) at least 6 months on haemodialysis; (ii) clinically with no acute illness in the 3 months preceding the start of the study; (iii) diuresis <1000 ml/day. Patients who did not fulfil any of these conditions were excluded from the study.

Complete data were obtained from 574 patients; there were 318 male and 256 female patients, and the mean age was 56.4 ± 14.6 years (range 18–81 years). The length of time on dialysis was 76 ± 59 months (range 6–286 months). All patients were on thrice weekly haemodialysis. The duration of the dialysis procedure ranged from 9 to 15 h per week. The blood flow was between 250 and 350 ml/min and the dialysate flow was 500 ml/min. In all 84% of the patients were on bicarbonate and 16% on acetate; 49% were on antihypertensive therapy and 67.4% receiving recombinant human erythropoietin. Underlying renal diseases were: chronic glomerulonephritis (24.2%), interstitial nephritis (18.8%), nephroangiosclerosis (12.5%), adult polycystic disease (9.3%), diabetes (8.6%), others (10.1%) and unknown (6.5%).

Methods

At the start of the study, significant comorbid medical problems which could influence the nutritional status or the outcome were inventoried. They included: cardiovascular disease (angina pectoris, congestive heart failure, myocardial infarction and peripheral vascular diseases), musculoskeletal disease (hyperparathyroidism, aluminium poisoning), neurological disease (stroke, transient ischaemic attacks, seizures, dementia), liver disease (chronic hepatitis and cirrhosis), hypertension (patients on antihypertensive therapy), primary renal disease (diabetes, nephroangiosclerosis) and social conditions. Each comorbid medical problem was assigned 0 points when the condition was not present and 1 point when it was. The points were totalled for each patient to obtain a comorbidity index.

Anthropometric measurements were performed using standard techniques [6,28–30] and included: height, weight, body mass index (BMI), i.e. weight divided by height squared, triceps skinfold thickness (TSF), mid-arm circumference (MAC), mid-arm muscle circumference (MAMC). The non-dominant arm was chosen for these measurements, unless that arm contained a vascular access site, in which case the other arm was used. Skinfold thickness was measured by a Harpender skin caliper. The measurements were performed in each unit by the same trained person after the midweek haemodialysis session, who followed precise written instructions. To assess the reproductivity of anthropometric measurements, four different observers performed the measurements on 30 patients in 2 consecutive weeks. The inter- and intra-observer coefficients of variation for TSF were $<10\%$ in both cases. The BMI, TSF, MAC and MAMC of the patients were compared with data obtained from normal Spanish adults of similar age and sex [31,32]. There were some differences from those of the American population [33]; TSF values were 25–35% lower in the Spanish population than in the American population, MAC values were only 5–10% lower in the Spanish population and MAMC values were 4.9% lower in Spanish men but similar in women. Normal parameters were defined when they were $>90\%$ of the 50th percentile of the controls. Mild decreases were defined by parameters of 80–90% of the 50th percentile of the controls. Moderate decreases were defined by a BMI of 70–79%, as well as TSF, MAC and MAMC of 60–79%. Severe decreases were defined by the BMI $<70\%$, and TSF, MAC and MAMC $<60\%$ of the 50th percentile.

Routine biochemical parameters were measured in blood drawn immediately before the first treatment of the week from the arteriovenous access and the following determinations were performed: haematocrit, haemoglobin, total lymphocyte count, blood urea nitrogen (BUN), serum creatinine, electrolytes, total protein, serum albumin, transferrin, pre-albumin. Plasma amino acids were measured in only 200 randomly selected patients. Measurements, except for plasma amino acids, were performed in the laboratory at each patient's centre on plasma or serum. Serum albumin was determined by a bromcresol method (normal range 3.4–5 g/dl).

A scoring system described by Bilbrey and Cohen [13] was used to quantify the degree of malnutrition. Eight parameters from the anthropometric (BMI, TSF, MAC, MAMC), labor-

atory (serum albumin, serum transferrin and lymphocytes) and clinical examination were used and each of them was given a score of 3 if normal and 4, 5, 6 if mildly, moderately or severely decreased respectively. The score ranged from a minimum of 24 to a maximum of 48. Four categories were defined according to the score: normal ($\leqslant 25$), mild malnutrition (26–28), moderate malnutrition (29–33) and severe malnutrition ($\geqslant 32$).

The dialysis dose was evaluated by the following parameters: hours of dialysis per week, midweek BUN, Kt/V and protein catabolic rate (PCR). Kt/V was calculated as the natural logarithm of BUN 1/BUN 2 and the effects of ultrafiltration were not considered. PCR was calculated as described [34,35].

$$\text{PCR (g/day)} = 9.35\ \text{G} + 0.294\ \text{V} \quad (1)$$

$$\text{G (mg/min)} = [\text{BUN } 3 - \text{BUN } 2)\ \text{V (dl)/T (min)}$$

V (total body water) was calculated by the equations proposed by Watson *et al.* [36].

*Male: V (1) = 2.447 − 0.09516 A (year) + 0.01074 height (cm) + 0.3362 weight (kg).

*Female: V (1) = −2.097 + 0.1069 height (cm) + 0.2466 weight (kg).

Normalized PCR [PCRn] to lean body mass to actual body weight, and to ideal body weight [PCRibw] were also calculated.

Statistical analysis

Values were expressed as mean ± SD. Each parameter represented the mean of two or three measurements performed in consecutive months. The χ^2 test was used to compare categorical data, and the Student's and the Mann–Whitney tests were performed when indicated. Multiple logistic regression models were used to determine the adjusted effect of the binary independent variables on nutritional status, mortality and morbidity [37,38]. In each case, the variables included in the model were those that have the most significant relationship to the dependent outcome in the univariate analysis (P value for the variable to be included should be no greater than 0.1). For malnutrition (yes = 1, no = 0), the variables included in the maximum model were age, gender, time on dialysis, comorbidity index, serum creatinine, hours of dialysis and PCRibw. For mortality (yes = 1, no = 0), the variables in the maximum model were age, comorbidity (cardiovascular, neurological, nephroangiesclerosis), MAMC, total lymphocyte count, serum albumin, serum creatinine and the nutritional index. For hospitalization (yes = 1, no = 0), the variables included in the maximum model were age, gender, the comorbidity index, serum albumin, serum creatinine and the nutritional index. Backward stepwise elimination was used to reduce the models to the subgroups of factors that made statistically significant contribution to nutritional status, mortality and morbidity (regression coefficient, $P < 0.05$).

Results

Prevalence of malnutrition

The anthropometric characteristics of the patients are shown in Table 1. The majority of stable patients on dialysis presented some alteration in the anthropometric measurements when compared with the control population. TSF was the most frequently altered parameter in both sexes: 41.2% men and 41.4% women had moderate or severe reductions (<80% of the standard 50th percentile), but moderate/severe reductions in MAMC (<80% of the standard 50th percentile) predominated in men (19.8% compared with 8.2%, $P < 0.001$) indicating a more severe depletion of proteins (Table 2). The majority of patients (440 patients or 76.6%) had serum albumin levels >40 g/l, 117 patients (20.4%) had levels of 35–40 g/l and only 17 patients (3%) had serum albumin levels <35 g/l. Transferrin was decreased in 34.5% of patients (<2 g/l). Total lymphocyte count was $< 1500 \times 10^6$/l in 57.3% of the patients and $< 1200 \times 10^6$/l in 32.9%. According to the malnutrition index, 80% of patients had some degree of malnutrition; it was mild in 30%, moderate in 22%, severe in 28% and there was no evidence of malnutrition in 20% . The prevalence of moderate/severe malnutrition (malnutrition index >28) in both sexes was 52.8% in males and 47.9% in females.

Data from patients without malnutrition (malnutrition index <28) and with moderate–severe malnutrition (malnutrition index >28) are shown in Table 3. Among the biochemical measurements not included in the nutritional index, no differences were found in the levels of total proteins, and branched chain amino

Table 1. Anthropometric measurements. Values are mean ± SD

	Male ($n = 318$)	Female ($n = 256$)	P
Age (years)	56.4 ± 14.6	56.2 ± 14.5	0.847
Weight (kg)	63.5 ± 9.4	58.6 ± 11.5	<0.001
Height (cm)	164.7 ± 7.7	153.2 ± 7.6	<0.001
BMI (kg/m^2)	23.4 ± 3.2	24.9 ± 4.8	<0.001
TSF (mm)	11.0 ± 6.5	17.5 ± 8.4	<0.001
MAC (cm)	26.1 ± 2.8	27.1 ± 4.3	<0.01
MAMC (cm)	22.5 ± 2.6	21.6 ± 3.8	<0.001

Abbreviations: BMI, body mass index; TSF, triceps skinfold thickness; MAC, mid–arm circumference; MAMC, mid–arm muscle circumference.

Table 2. Prevalence of alterations in anthropometric measurements. Figures in parentheses are percentages

	Normal	Mild	Moderate	Severe
BMI				
male	150 (47.2%)	105 (33.0%)	56 (17.6%)	7 (2.2%)
female	158 (61.7%)	68 (26.6%)	25 (9.8%)	5 (1.9%)
TSF				
male	152 (47.8%)	35 (11.0%)	66 (20.8%)	65 (20.4%)
female	120 (46.9%)	30 (11.7%)	44 (17.2%)	62 (24.2%)
MAC				
male	162 (50.9%)	93 (29.2%)	63 (19.8%)	0 (0.0%)
female	158 (61.7%)	63 (24.6%)	34 (13.3%)	1 (0.4%)
MAMC				
male	132 (41.5%)	123 (38.7%)	60 (18.9%)	3 (0.9%)
female	176 (68.8%)	59 (23.0%)	19 (7.4%)	2 (0.8%)

Abbreviations: BMI, body mass index; TST, triceps skinfold thickness; MAC, mid-arm circunference; MAMC, mid-arm muscle circumference.

Table 3. Characteristics and nutritional status of patients*. Values are mean ± SD

	Normal ($n=296$)	Malnutrition ($n=278$)	P
Sex (m/f)	154/142	164/114	0.128
Age (yr)	55.6 ± 14.6	57.1 ± 14.7	0.176
Time on HD(months)	65.8 ± 52.3	86.8 ± 63.6	<0.001
Comorbidity index	1.4 ± 1.1	1.8 ± 1.4	<0.001
EPO treatment (No/Yes)	95/201	92/186	0.745
Hct (%)	32.1 ± 4.7	31.6 ± 5.0	0.319
BUN (mmol/l)	28.6 × 6.0	28.2 ± 6.0	0.433
SCr (umol/l)	1109 ± 230	937 ± 221	0.001
Total proteins (g/l)	69.7 ± 5.6	69.9 ± 5.5	0.630
Serum albumin (g/l)	42.1 ± 4.0	41.3 ± 4.1	0.111
Serum transferrin (g/l)	2.3 ± 0.6	2.2 ± 0.5	<0.01
Total lymphocyte count ($\times 10^6$/l)	1606 ± 597	1378 ± 542	<0.01
Plasma valine (umol/l)	188 ± 56	185 ± 50	0.298
Plasma isoleucine (umol/l)	63 ± 22	59 ± 17	0.130
Plasma leucine (umol/l)	108 ± 40	113 ± 52	0.291
Duration of HD (h/week)	10.2 ± 1.6	9.9 ± 1.4	<0.05
Kt/V	1.08 ± 0.20	1.10 ± 0.21	0.103
PCRibw (g/kg/day)	1.02 ± 0.22	0.94 ± 0.18	<0.001
Malnutrition index	26.0 ± 1.4	32.5 ± 2.9	<0.001

*Patients with moderate or severe malnutrition according to the malnutrition index (>28) had several differences from those with higher values of the index. Plasma amino acid determinations were performed in 90 patients with normal nutritional status and in 82 patients with malnutrition.
Abbreviations: HD, haemodialysis; EPO, erythropoietin; Hct, haematocrit; BUN, blood urea nitrogen; SCr, serum creatinine; PCRibw, protein catabolic rate normalized to ideal body weight.

Table 4. Results of the multiple logistic regression analysis to identify predictors of malnutrition

	Odds ratio	95% Confidence interval	P
Age (>65 years = 1)	1.96	1.22–3.14	0.005
Sex (male = 1)	1.95	1.24–3.07	0.004
Comorbidity index	1.23	1.03–1.45	0.017
Time on HD (years)	1.13	1.08–1.18	<0.001
Duration of HD (h)	0.73	0.63–0.85	<0.001
PCRibw (g/kg/day)	0.17	0.06–0.50	<0.001

Abbreviations: HD, haemodialysis; PCRibw, protein catabolic rate normalized to ideal body weight.

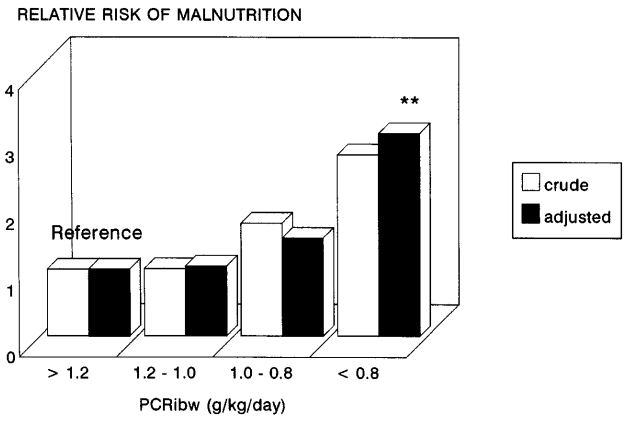

Fig. 1. Comparison of crude and adjusted relative risk of malnutrition for groups of patients with different protein intake measured by the protein catabolic rate normalized to ideal body weight (PCRibw). $^{**}P<0.01$ compared with reference.

acids: valine, isoleucine and leucine. Moreover, no differences were observed in some parameters evaluating the amount of dialysis (midweek BUN, KT/V and PCR normalized to lean and actual body weight) and the nutritional status. However, the length of weekly haemodialysis and PCR normalized to ideal body weight were lower in the group of patients with malnutrition. Some biochemical parameters such as serum creatinine ($r=-0.190$, $P<0.001$), and PCRibw ($r=-0.183$, $P<0.001$), showed a low, negative, but significant correlation with the malnutrition index. Furthermore, serum albumin was positively correlated with serum creatinine concentration ($r=0.325$, $P<0.001$) and negatively with the comorbidity index ($r=-0.168$, $P<0.001$).

The multiple logistic regression analysis showed that six independent variables influenced the nutritional status: age, gender, time on dialysis, comorbidity index, hours of dialysis and PCR normalized to ideal body weight (Table 4). Gender increased the significance when the model was adjusted by hours of dialysis and PCRibw. Hours of dialysis and PCRibw were powerful predictors of risk. When compared with a reference PCR of 1.2 g/kg/day, patients with lower PCR values had progressively increased odds ratios for malnutrition (Figure 1).

Evolution after 1 year follow-up

After 1 year of follow-up, complete information on 84 patients was not available and 48 patients had received a transplant. The analysis of morbidity and mortality was conducted using data from the remaining 442 patients. Of the patients, 68 (15.4%) had died during the year of follow-up. The characteristics of the patients according to the outcome are expressed in Table 5. Age and the comorbidity index were higher in the dead patients who had a greater frequency of diabetes and nephroangiosclerosis. MAMC was lower in the dead patients than in those patients alive after 1 year of follow-up. Among the biochemical measurements, only lymphocytes, serum creatinine and serum albumin showed differences between the dead and live patients.

Cardiovascular disorders accounted for 57.3% of total deaths, followed by infection (10.4%), malignancies (5.9%) and other causes (20.6%). Only four patients (5.9%) died of cachexia. Multiple logistic regression analysis was performed to investigate the predictors of death, and the results are summarized in Table 6. Age, cardiovascular disease, neurological diseases, nephroangiosclerosis and total lymphocyte count were found to be the only significant predictors of death. Anthropometric and biochemical parameters were not significant predictors of death.

Morbidity was evaluated by the hospitalization rates. There were 309 hospitalizations and 195 patients (44.1%) needed hospitalization during the year of

Table 5. Characteristics associated with mortality. Values are mean ± SD. Values of diabetes and hypertension are those with/those without

	Survived ($n=374$)	Died ($n=68$)	P
Age (years)	56.4 ± 14.0	65.8 ± 10.9	<0.001
Sex (m/f)	204/170	39/29	0.725
Time on HD (months)	80.5 ± 61.5	76.1 ± 59.8	0.576
Comorbidity index	1.6 ± 1.3	2.3 ± 1.4	<0.001
Nephroangiosclerosis (no/yes)	336/38	51/17	<0.01
Diabetes (no/yes)	345/29	56/12	<0.05
Hypertension (no/yes)	180/194	39/29	0.186
BMI (kg/m^2)	24.3 ± 4.0	24.5 ± 4.5	0.758
TST (mm)	13.7 ± 8.1	14.3 ± 8.1	0.562
MAC (cm)	26.7 ± 3.6	25.9 ± 3.9	0.144
MAMC (cm)	22.3 ± 3.4	21.5 ± 3.0	0.041
SCr (umol/l)	1008 ± 247	989 ± 241	<0.001
Serum albumin (g/l)	42 ± 3.9	40 ± 5.0	0.033
Total lymphocyte count ($\times 10^6$/l)	1584 ± 594	1261 ± 530	<0.01
Malnutrition index	29.1 ± 3.9	30.7 ± 4.5	<0.01

Abbreviations: BMI, body mass index; TSF, triceps skinfold thickness; MAC, mid-arm circumference; MAMC, mid-arm muscle circumference; SCr, serum creatinine.

Table 6. Results of the multiple logistic regression analysis to identify predictors of death

	Odds ratio	95% Confidence interval	P
Age (years)	1.06	1.03–1.09	<0.001
Cardiovascular disease (Yes = 1)	2.13	1.19–3.83	0.011
Neurological disease (Yes = 1)	2.96	1.41–6.16	0.003
Nephroangiosclerosis (Yes = 1)	2.34	1.10–4.98	0.027
Total lymphocyte count (100 cells/mm^3)	0.93	0.87–0.98	0.016

follow-up. The admission rates were computed as the total number of hospital admissions divided by the total number of patients years at risk. Hospital days per patient year were computed as the total number of hospital days divided by the number of patient years at risk. The overall rates of hospital admissions and hospital days per patient year at risk are presented in Table 7. Females had higher hospital days per patient year at risk than males. Hospital admission rates and hospital days per patient year at risk increased with age, with comorbidity with hypoalbuminaemia and with malnutrition.

Logistic regression analysis showed three predictors of hospitalization; the comorbidity index [odds ratio 1.37, 95% confidence interval (CI) 1.16–1.60, $P<0.001$], serum albumin (odds ratio 0.51, 95% CI 0.31–0.84, $P<0.01$) and age (odds ratio 1.015, 95% CI 1.001–1.03, $P<0.05$).

Discussion

The prevalence of moderate/severe malnutrition in our patients was 48%, which is fairly high despite the patients being in a stable clinical condition. However, a similar frequency of alterations on anthropometric and biochemical measurements and nutritional status have been reported [7,9,13,39]. Fat depletion, estimated by decreases of TSF, was the predominant type of malnutrition in both sexes [7,9,10]. These findings differ from those of Bilbrey *et al.* [13] who found a better preservation of triceps skinfold thickness in men, using the same malnutrition criteria. Moderate protein depletion estimated by decreases of MAMC was also present in 20% of the male patients. It has been demonstrated that patients on haemodialysis have a similar energy expenditure and requirements as normal individuals [40,41]. However, dialysis patients usually eat lower amounts of calories than recommended, although the intake of proteins is closer to prescribed levels [7–10]; this could contribute to fat depletion. The differences in the prevalence of malnutrition in the different studies could be due to the method used in the assessment of malnutrition. Assessing nutritional status is difficult as there is not a single test that can be considered an indicator of protein–calorie malnutrition. It has been suggested that an assessment of malnutrition should rely on multiple indices of nutritional status, these indices comprising several biochemical measures, including serum albumin, as well as an analysis of body composition [42]; however, no definitive criteria have been established. Among the indices commonly used, serum proteins such as albumin and transferrin, may be depressed by non-nutritional factors even in haemodialysis patients [26,27,43]. The main criticism of anthropometric measurement is a lack of precision for an individual patient [28,43]. However, Nelson *et al.* [30] have shown that anthropometry can be reproducible and that its sensitivity has a 90% threshold. In our study, the inter- and intra-observer coefficients of variation for TSF were ~10%

Table 7. Factors associated with hospitalization

	Admission rates per patient year at risk	Hospital days per patient year at risk
All patients ($n=442$)	0.83	6.45
Sex		
Male ($n=242$)	0.85	5.87
Female ($n=200$)	0.86	9.97
Age (years)		
<65 ($n=293$)	0.69	7.26
≥65 ($n=149$)	0.87	8.65
Comorbidity index		
0 ($n=67$)	0.58	6.55
1–3 ($n=338$)	0.89	8.81
>3 ($n=37$)	1.54	17.03
Malnutrition		
No ($n=90$)	0.47	6.55
Mild ($n=133$)	0.77	7.11
Moderate ($n=85$)	0.67	6.74
Severe ($n=134$)	1.13	11.64
Serum albumin		
≥40 g/l ($n=329$)	0.63	6.76
<40 g/l ($n=113$)	1.12	10.51

and the variance studies did not show differences among the measurements performed by four observers in the same individuals.

We have not be able to find a published report that includes an analysis investigating factors associated with the development of malnutrition. In our study, male sex, time on dialysis, weekly duration of dialysis and PCRibw were the most important predictors of malnutrition. PCRibw values of <1.0 g/kg/day increased the risk of malnutrition by 1.47, and when the PCRibw was <0.8 g/kg/day, the risk of malnutrition was three-fold the reference value after adjusting for other variables. PCR normalized to lean body mass [PCRn] and PCR related to actual body weight did not predict malnutrition, probably because these parameters may overestimate the protein intake of malnourished patients and underestimate the protein intake of obese patients or of those without malnutrition [44]. Our findings may mean that PCRibw is also an indirect estimate of calorie intake. Importantly, duration of dialysis and PCRibw are the only predictors of malnutrition which could be modified by nutritional intervention.

Life expectancy in patients undergoing haemodialysis is markedly reduced [45]. Demographic factors such as age, race and cause of end stage renal disease, comorbid conditions at the start of treatment and several biochemical parameters such as serum albumin, serum creatinine and serum cholesterol have been identified as predictors of mortality in these patients [18–25,46–58]. The predictors of death in our patients were: age, comorbidity (cardiovascular and neurological diseases), nephroangiesclerosis as the cause of primary renal disease and total lymphocyte count. Age was the most important predictor as has been reported in the vast majority of previous studies [18,20–23,47–52,54–58]. However, in this cross-sectional study of Spanish patients, unlike those in North America, anthropometric parameters [13,51] and biochemical measurements [20–25,52,58] were not identified as predictors of death and most of them were not included in the logistic regression model. The only nutritional parameter predictive of mortality was total lymphocyte count. But as with other measurements, several factors related to patient status and the haematological situation can affect results and no definitive data allow a lowered total lymphocyte count to be attributed to protein–calorie malnutrition [29].

Serum albumin was not a predictor of mortality in our patients, as in other studies [57,58,59]. The discrepancy with results from North American dialysis patients [20–25] could be explained by the differences in the patients, the length of the follow-up and the small number of patients with hypoalbuminaemia. The serum albumin concentration was normal in the majority of our patients as in the National Cooperative Dialysis Study population [9] and in recently published series from Italy [57,60,61]. Several studies have described serum albumin levels <4 g/dl in 66% of patients on haemodialysis [20] and <3.5 mg/dl in 14–50% [7,20,24,25,52]. In these series serum albumin was determined by the bromcresol green, the method used in our study, so the differences we describe can not be due to the method of measuring serum albumin [62]. Regarding differences in patients, we studied stable patients, with >6 months in haemodialysis to identify the impact of nutritional factors rather than acute illness. For example, death rates of 12% can occur during the first 90 days of haemodialysis therapy and such patients have lower values of serum albumin than those who survive [63]. However, the significance of hypoalbuminaemia in such patients is not clear: it has been attributed to insufficient protein intake [64], or an acute response from a disease process [65], or to increased vascular permeability [66,67], or inflammatory state [68]. Kaysen *et al.* [26] found that hypoalbuminaemia in haemodialysis patients is due to decreased albumin synthesis associated with non-nutritional factors.

Cardiovascular diseases were the leading cause of death and infection was the second most important cause of death in our series as in other series [18,25,54,56,69] . Only four patients died of cachexia; these patients were older, had several comorbid factors, and cachexia was considered as a final event. Hospital admission rates and hospital days per patient year at risk were lower than those reported in other series [52,70–73]. The reason for this difference is unknown but it is likely to be due in part to exclusion of patients in the first months of dialysis therapy. Age, the comorbidity index and serum albumin were the only predictors of hospitalization [17], as in mortality no other nutritional measurement was identified as a increasing risk factor.

In summary, malnutrition, estimated by anthropometric and biochemical measurements was a frequent complication in Spanish haemodialysis patients. Fat depletion predominated in both sexes, but protein depletion was present in 20% of males. Age >65 years, time on dialysis, comorbidity, weekly duration of dialysis and PCRibw were the predictors of malnutrition. The mortality rate was 15.4% in this selected group of patients; age at the time of study, comorbid conditions related to vascular diseases and total lymphocyte count were the predictors of death, and cardiovascular diseases were the most important causes. Hospitalization needed in 44% of patients was related to comorbidity, serum albumin and age. Although total lymphocyte count was a predictor of mortality and serum albumin of hospitalization, the fact that malnutrition is a risk factor to mortality and morbidity is not clearly established.

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