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Original Article

A comparative analysis of nutritional parameters as predictors of outcome in male and female ESRD patients

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Abstract

Background. Many patients with end-stage renal disease (ESRD) are malnourished and cross-sectional studies show that markers of malnutrition may predict death. Serum albumin (S-albumin), the commonest nutritional marker, has been criticized because it is so closely related to the effects of inflammation and other non-nutritional factors. Consequently, we need other nutritional markers that can predict outcome. However, males and females differ as regards body composition and it is not known how this may influence the predictive power of different nutritional markers.

Methods. In 206 ESRD patients (126 males) aged 52 ± 1 years, we evaluated the relationship between survival and five estimates of nutritional status (S-albumin, subjective global assessment (SGA), lean body mass (LBM), body fat mass (FM) assessed by dual-energy X-ray absorptiometry, and handgrip strength (HGS)) close to start of renal replacement therapy (RRT). The patients were also classified as regards the presence of cardiovascular disease (CVD), diabetes mellitus (DM), and inflammation (CRP $\geqslant$ 10 mg/l). Mortality was monitored over mean follow-up period of 37 ± 2 months.

Results. In the whole patient group, the presence of CVD, DM, inflammation, and malnutrition (SGA > 1) close to start of RRT all predicted poor outcome. However, whereas inflammation strongly predicted ($P < 0.0001$) poor outcome in males, no such effect was observed in females. Also, differences were found between males and females regarding the predictive value of the five different nutritional estimates. Whereas HGS, SGA, and S-albumin independently predicted poor outcome in males, only SGA predicted outcome (independently of age, CVD, and DM) in females.

Conclusions. Mild to moderate malnutrition, as assessed by SGA, was present in 39% of the patients and predicted outcome independently of age and co-morbidity in both males and females. However, the predictive power of various other nutritional markers differed markedly between male and female patients. Whereas a low HGS was an excellent independent outcome predictor in males, no predictive power of this parameter was found in females. S-albumin is more closely related to co-morbidity and inflammation than nutritional status in patients close to start of RRT. We conclude that sex is an important factor that must be taken into account in studies on nutrition and nutritional interventions in ESRD patients.

Keywords: end-stage renal disease; handgrip strength; inflammation; malnutrition; sex

Introduction

Protein-energy malnutrition and wasting are common among patients with end-stage renal disease (ESRD) [1–3]. Moreover, considerable evidence has accumulated over several years that malnutrition in dialysis patients is associated with poor survival [4–6]. Although various factors associated with the dialysis procedure *per se*, such as bio-incompatibility and nutrient losses, may contribute to malnutrition, recent studies have shown that malnutrition is common even before start of dialysis [1,3,5]. The decline in nutritional status during the course of renal failure may be caused by disturbances in protein and energy metabolism, hormonal derangements, as well as a spontaneous reduction in dietary energy and protein intake [7]. However, apart from uraemic toxicity, several co-morbid conditions may also contribute to malnutrition among ESRD patients. In particular, chronic inflammation, cardiovascular disease (CVD), diabetes mellitus (DM), and other superimposed illnesses can produce anorexia and malnutrition.

Currently, although several approaches (based on clinical evaluation, anthropometric measurements as

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well as biophysical and biochemical methods) have been used to assess nutrition, S-albumin is probably still the most commonly used nutritional marker in ESRD patients. However, its value has been questioned because a low S-albumin level may reflect not only poor nutrition, but also albumin losses in urine (and/or dialysate), presence of an inflammatory reaction, systemic diseases, old age, and degree of hydration [8–10]. Since the prevalence of inflammation is reportedly high (30–50%) in ESRD patients [11], inflammation may be one important cause of hypoalbuminaemia [12]. Therefore, chronic inflammation rather than poor nutritional intake might cause the previously reported association between hypoalbuminaemia and mortality. As S-albumin is very vulnerable to the effects of inflammation and systemic disease(s) [13], it is obvious that other parameters are needed to assess nutritional status. Ideally, a nutritional marker should not only be an inexpensive and easily performed bedside test, but inflammation and various systemic diseases should also not affect it. Unfortunately, no such ideal nutritional marker is available today. Several methods have been used to monitor lean body mass (LBM), e.g. anthropometrics, creatinine kinetics, bioimpedance, and dual-energy X-ray absorptiometry (DXA). Of these, DXA seems to be the most reliable, especially if serial measurements are made [14]. By using DXA, a reliable estimation of the amount of body fat mass (FM) can also be done. However, DXA is not widely available. Recently, we reported that handgrip muscle strength (HGS), a simple and easily performed bedside test, correlated well with LBM in ESRD patients [10]. However, we do not know whether HGS is also a reliable predictor of outcome in ESRD patients.

In the present study, we evaluated the predicted outcome of co-morbidity, inflammation, and five different nutritional markers (S-albumin, subjective global assessment (SGA), HGS, LBM, and FM) measured shortly before start of RRT in 206 patients. Since sex markedly affected various nutritional parameters, such as LBM, FM, and HGS, we analysed the data in males and females separately to determine whether sex affects the predictive power of various nutritional markers on outcome.

Subjects and methods

Patients

Two-hundred-and-six patients (126 males) with ESRD were studied close to start of dialysis. Exclusion criteria were age >70 years and unwillingness to participate in the study. They were included in an ongoing prospective study and some of the data have been reported elsewhere [3,10]. The cause of ESRD was diabetic nephropathy in 62 patients (30%), chronic glomerulonephritis in 57 (28%), polycystic kidney disease in 22 (11%), and other (or unknown) aetiologies in 65 patients (31%). Most of them were taking antihypertensives (beta-blockers, calcium channel blockers, furosemide, and/or ACE-inhibitors) as well as other drugs commonly used in ESRD, such as phosphate-binders, potassium-binders, and vitamin B, C and D supplements. Sixty-seven patients (33%) had clinical signs of cerebrovascular, cardiovascular, and/or peripheral vascular disease; grouped here as CVD. Thus, 17 had suffered from cerebrovascular disease, 20 one or more myocardial infarctions, 22 had clinical signs of ischaemic heart disease, 20 peripheral ischaemic atherosclerotic vascular disease, and 4 patients had had aortic aneurysm.

After an overnight fast, serum samples for analysis of S-albumin, C-reactive protein (CRP), and S-creatinine were taken. Nutritional status was assessed by determining weight, SGA [15], and HGS (evaluated in both the dominant and non-dominant arms using the Harpenden dynamometer). Handgrip strength was repeated three times and the highest value was noted. Since many patients had an AV-fistula in the non-dominant arm, the data from the dominant arm were used in the analysis. Finally, LBM and FM were evaluated with DXA in 185 of the patients.

Estimated protein intake ($6.25\times[(0.028\times$urea excretion rate$)+(0.031\times$body weight$)]$ was 0.70 ± 0.01 g/kg ($n=166$), whereas energy intake was not assessed. One-hundred-and-thirteen patients (55%) started treatment with continuous ambulatory peritoneal dialysis (CAPD) and 87 (42%) started haemodialysis (HD). Three patients received a kidney transplant without starting dialysis treatment and three patients had not yet started dialysis. During the observation period, 55 patients (37 males) died. The mean time from examination to start of RRT was 34 ± 7 days (range -54 to 426 days). Survival was determined after a mean follow-up of 37 ± 2 months (range 0.7–83.8 months). The effects of age, gender, CVD, DM, as well as inflammation and five nutritional parameters (S-albumin, SGA, HGS, LBM, and FM) were determined with the Cox proportional hazard model and the relative risk of death was calculated. Survival was measured from the day of examination until death or censoring, which was made at the end of the follow-up (5 November 2001). Eighty-four patients received a kidney transplant subsequent to entering the study and were followed in the same way as those that did not receive a transplant. The Ethics Committee of Karolinska Institutet approved the study protocol at Huddinge University Hospital, Stockholm and informed consent was obtained from all patients.

Analyses and calculations

The DXA scan was performed with the DPX-L machine (Lunar Corp., Madison, WI, USA), and the data evaluated using Lunar software version 3.4. With this technique, bone mineral, fat, and LBM distribution are directly estimated without making assumptions about the two-compartment model. DXA has proved superior to other simple non-invasive methods for determining body composition in renal failure, especially if repeated measurements are made [14]. However, it must be kept in mind that, although the state of hydration does not affect the estimate of FM with DXA, it does affect that of LBM.

Determinations of S-albumin (bromcresol purple method), CRP, S-creatinine, and urinary creatinine were carried out in the Department of Clinical Chemistry, Huddinge Hospital, using routine methods. At the start of the study (1994), the detection limit of CRP was 10 mg/l in the Department of Clinical Chemistry, Huddinge Hospital and all values <10 mg/l were treated as 9 mg/l in the statistical evaluation.

Statistical methods

Values are presented as mean ± SEM or medians with $P < 0.05$ taken to indicate significance. The two groups were compared with the Student's t-test or Mann–Whitney U-test as appropriate. Comparisons between two groups for nominal variables were made with Fisher's exact test. Correlations were determined with linear regression analysis (r) for normally distributed variables and Spearman's rank (ρ) for not-normally distributed variables. Independent associations between one dependent variable and more than two independent variables were assessed with stepwise multiple regression analysis. Survival analyses were made with Kaplan–Meier or Cox regression analyses.

Results

Basal nutritional data

The basal clinical characteristics of the male and female ESRD patients close to start of dialysis are given in Table 1. One-hundred-and-nineteen of them were classified as well-nourished (SGA 1) and the rest showed signs of mild (SGA 2, $n = 64$) or moderate (SGA 3, $n = 13$) malnutrition. The SGA scoring was missing in 10 patients. For the statistical evaluation, the findings in SGA 2 and 3 were grouped together as SGA >1. Age, glomerular filtration rate and prevalence of malnutrition, CVD, DM, and inflammation (CRP >10 mg/l) were similar in male and female ESRD patients. As expected, female ESRD patients had significantly lower body weight, LBM, S-creatinine levels, and HGS, but their FM was significantly higher.

Table 1. Baseline clinical characteristics of men and women included in the study

	Men	Women	*P* value
Number	126	80	
Age (years)	52.0 ± 1.0	52.0 ± 1.0	NS
Observation period (months)	37.0 ± 2.0	37.0 ± 3.0	NS
Body weight (kg)	76.6 ± 1.2	66.0 ± 1.7	<0.0001
LBM (kg)[a]	55.5 ± 0.7	39.2 ± 0.7	<0.0001
Body fat mass (kg)[a]	19.1 ± 0.7	25.1 ± 1.4	<0.0001
Serum albumin (g/l)	33.0 ± 0.6	32.7 ± 0.7	NS
Serum creatinine (μmol/l)	729.0 ± 22.0	605.0 ± 21.0	<0.001
Creatinine clearance (ml/min)[b]	7.0 ± 1.0	7.0 ± 1.0	NS
HGS (kg)[c]	37.0 ± 1.0	23.0 ± 1.0	<0.0001
Inflammation (CRP >10 mg/l)	38%	34%	NS
Malnourished (SGA >1)[d]	38%	41%	NS
CVD	36%	28%	NS
DM	32%	26%	NS

NS, not significant.
[a]Data missing in 21 patients.
[b]Data missing in 72 patients.
[c]Data missing in 37 patients.
[d]Data missing in 10 patients.

Associations between HGS and other nutritional parameters

Well-nourished (SGA 1) male (42 ± 1 *vs* 25 ± 2 kg, $P < 0.0001$) and female (29 ± 2 *vs* 20 ± 1 kg, $P < 0.05$) ESRD patients had significantly better HGS than their malnourished (SGA >1) counterparts. We found strong positive correlations between HGS and LBM in the entire patient material ($r = 0.70$, $P < 0.0001$) as well as in the male ($r = 0.54$, $P < 0.0001$) and female ($r = 0.38$, $P < 0.01$) sub-populations. Similarly, HGS and S-creatinine correlated positively in both males ($r = 0.42$, $P < 0.0001$) and females ($r = 0.39$, $P < 0.01$). Age was inversely correlated with HGS in both the male ($r = -0.39$, $P < 0.0001$) and female ($r = -0.35$, $P < 0.01$) patient groups. Weak, but significant, inverse correlations were found between HGS and CRP ($\rho = -0.20$, $P < 0.05$) and S-albumin ($r = 0.18$, $P < 0.05$), respectively, in the whole patient group.

Associations between S-albumin, co-morbidity and nutritional parameters

In the present study, significantly lower S-albumin levels were found in patients with CVD (30.7 ± 0.8 *vs* 33.9 ± 0.5 g/l, $P < 0.001$), DM (30.3 ± 0.8 *vs* 34.0 ± 0.5 g/l, $P < 0.001$) and inflammation (30.5 ± 0.6 *vs* 34.2 ± 0.6 g/l, $P < 0.001$) compared with patients without these complications. On the other hand, malnourished (SGA >1) ESRD patients did not have significantly (31.8 ± 0.7 *vs* 33.7 ± 0.6 g/l, $P = 0.06$) lower S-albumin levels than their well-nourished (SGA 1) counterparts. In a stepwise multiple regression model, including age, log CRP, CVD, DM, and two nutritional markers (SGA and LBM), only DM (F-ratio 7.4, $P < 0.01$) and log CRP (F-ratio 5.9, $P < 0.05$) were independently associated with S-albumin levels. Negative correlations were found between S-albumin and CRP among all patients ($\rho = -0.14$, $P < 0.0001$) and males ($\rho = -0.23$, $P < 0.0001$), but not in females ($\rho = -0.02$, $P = 0.07$). No correlation was found between estimated protein intake and S-albumin levels ($\rho = 0.08$, NS). Inverse correlations were found between S-albumin and age in the whole patient group ($r = -0.25$, $P < 0.001$), as well as in the male ($r = -0.26$, $P < 0.01$) and female ($r = -0.22$, $P = 0.05$) sub-populations. On the other hand, no significant correlations were found between S-albumin and S-creatinine or LBM in the whole patient group.

Associations between CRP, co-morbidity, and nutritional parameters

In the present study, a markedly higher prevalence of elevated CRP levels was found in patients with CVD (55% *vs* 27%, $P < 0.001$) and malnutrition (56% *vs* 23%, $P < 0.001$), whereas the prevalence of inflammation did not differ between patients with or without DM (39% *vs* 35%, $P = 0.75$). In a stepwise multiple regression model, including age, CVD, DM, and two nutritional markers (SGA and LBM), only age

(*F*-ratio 21.0, $P<0.001$) and SGA (*F*-ratio 8.9, $P<0.01$) were independently associated with log CRP levels. No significant correlations were found between CRP and LBM and S-creatinine, respectively, in the whole patient group.

Effects of gender, type of dialysis, co-morbidity, and inflammation on outcome

No difference in mortality rate was observed between males and females (log rank 0.9), whereas patients with CVD (log rank 57.5, $P<0.0001$) and DM (log rank 11.6, $P<0.001$) at start of RRT had a significantly higher mortality rate (Figure 1). When the patient material was divided according to gender, strong associations between the presence of CVD and outcome were observed in both males (log rank 34.3, $P<0.0001$) and females (log rank 22.0, $P<0.0001$). On the other hand, whereas diabetic men (log rank 8.5, $P<0.01$) had a worse outcome than non-diabetic men, no significant difference in survival (log rank 2.1, $P=0.15$) was observed between diabetic and non-diabetic females, respectively. No difference (log rank 0.0) in survival was observed between the different treatment modalities (HD *vs* PD) during the observation period (Figure 1). Inflamed patients (CRP $\geqslant 10$ mg/l) at start of RRT had a significantly higher (log rank 21.2, $P<0.0001$) mortality rate than non-inflamed patients (Figure 2). Thus, overall mortality was significantly higher during the observation period in patients with elevated CRP (41% *vs* 18%, $P<0.001$). However, if the patient material was divided according to sex, inflamed male patients had a significantly (log rank 24.3; $P<0.0001$) worse outcome, whereas no such effect (log rank 1.7) was observed among females (Figure 3). Likewise, whereas overall mortality was significantly higher during the observation period in inflamed males (48% *vs* 18%, $P<0.001$), no significant difference (30% *vs* 19%, $P=0.40$) in mortality rate was observed in females with or without inflammation, respectively.

Effects of different nutritional markers on outcome

In the whole patient material, 55 patients who died had significantly lower S-albumin levels at start of RRT (30.7 ± 0.9 *vs* 33.6 ± 0.5 g/l, $P<0.01$) than 151 survivors. Kaplan–Meier survival analyses showed that in the

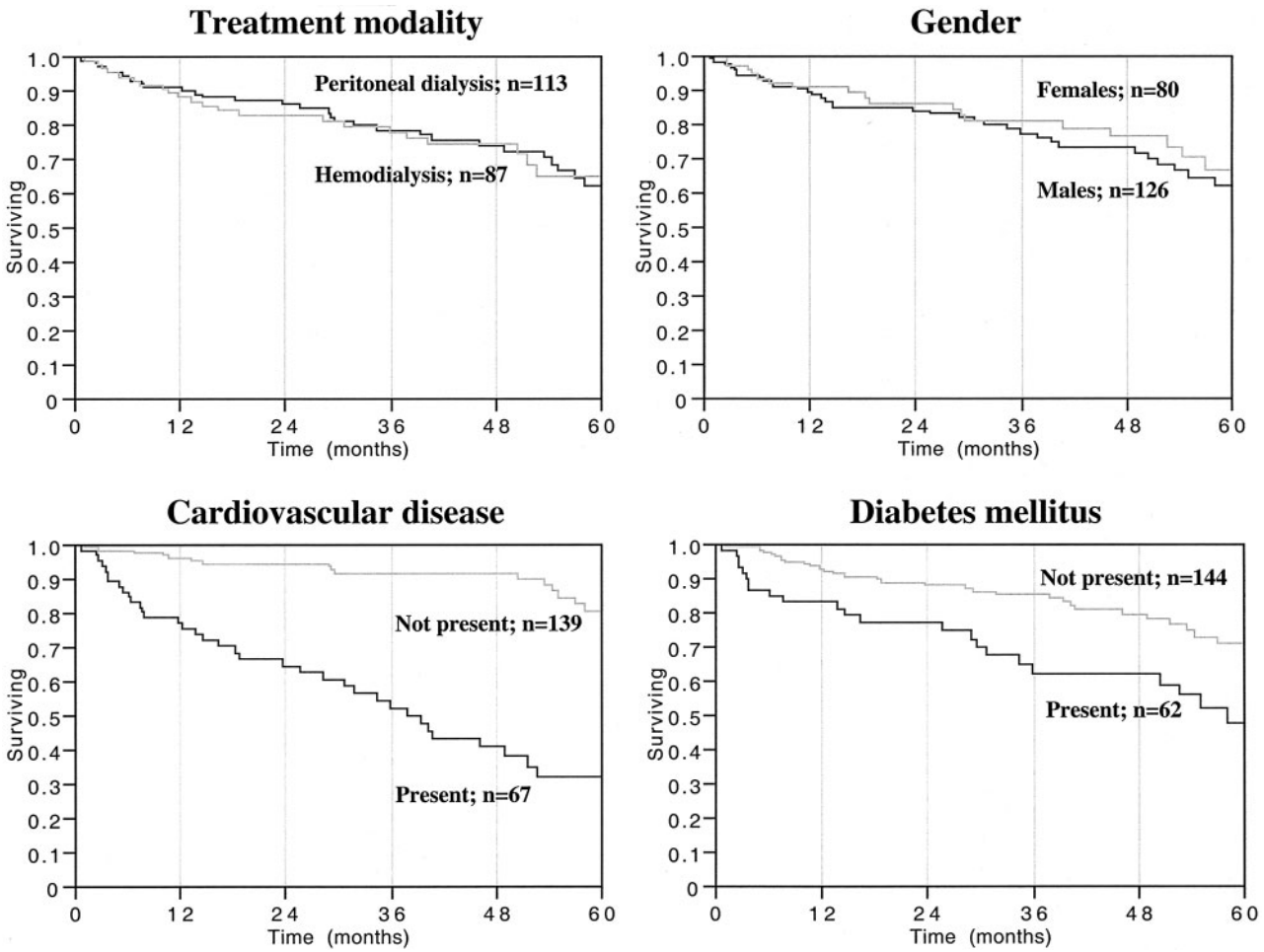

Fig. 1. Survival by Kaplan–Meier in all patients ($n=206$) according to treatment modality (log rank 0.0, NS), gender (log rank 0.9, NS), and the presence of CVD (log rank 57.5, $P<0.0001$) and DM (log rank 11.6, $P<0.001$) at start of RRT.

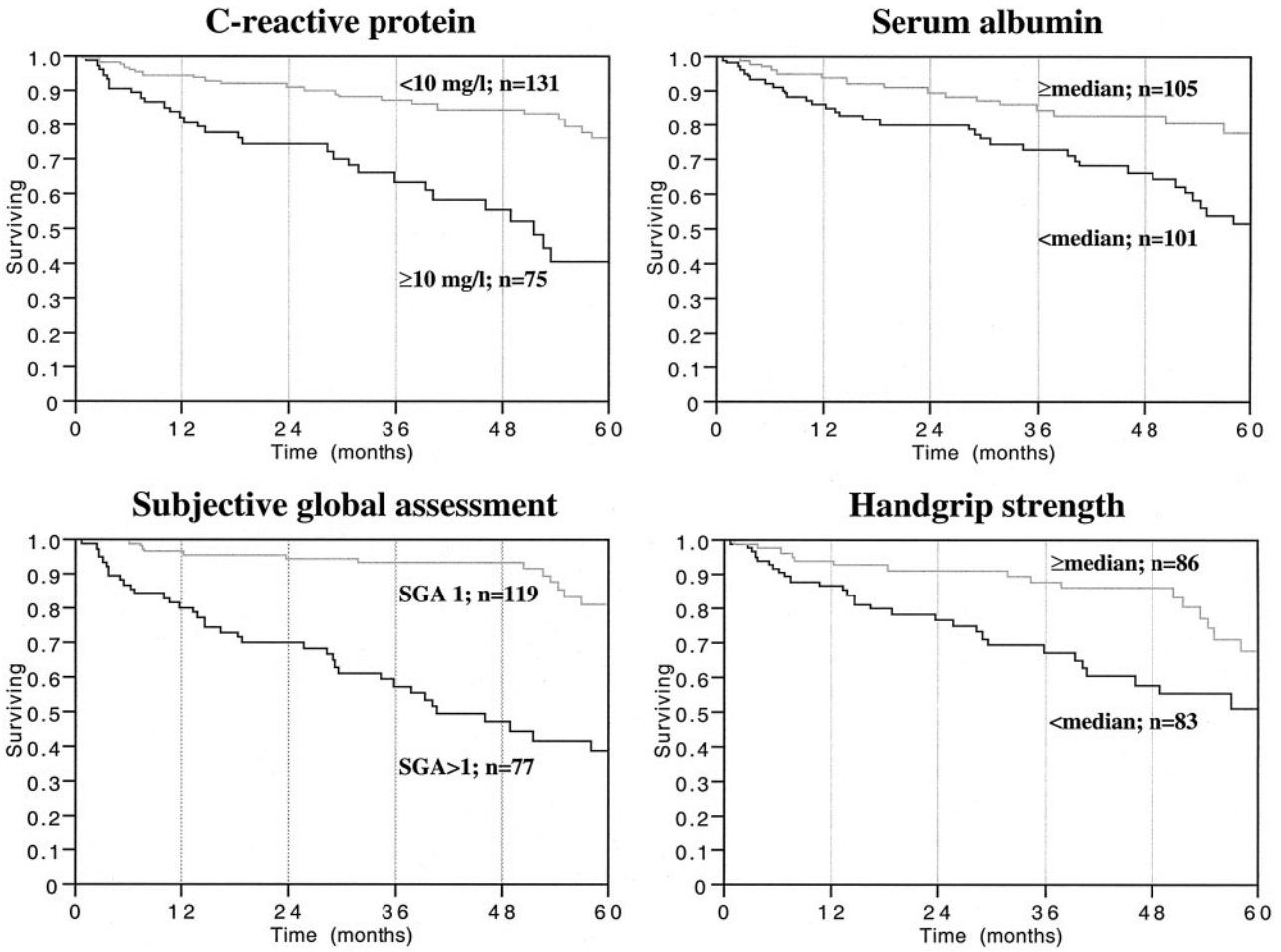

Fig. 2. Survival by Kaplan–Meier in all patients ($n=206$) according to the presence of inflammation (log rank 11.2, $P<0.0001$), S-albumin (log rank 9.6, $P<0.01$), SGA (log rank 44.2, $P<0.0001$), and HGS (log rank 7.2, $P<0.01$) evaluated at start of RRT.

entire group of patients with S-albumin levels above the median ($\geqslant 33$ g/l) the mortality rate was lower (log rank 4.9, $P<0.05$) than in those with S-albumin <33 g/l. A significant difference in outcome was found in males (log rank 7.3, $P<0.01$) but not in females (log rank 1.9, $P=0.16$) when the two groups were evaluated separately with regard to median S-albumin levels. The predictive power of S-albumin (hazard ratio 0.95, 95% CI: 0.91–0.98, $P<0.01$) was lost (hazard ratio 0.96, 95% CI: 0.92–1.00, $P=0.06$) if correction were made for the impact of age and CRP.

We also studied prospectively the predictive power of four other nutritional parameters (SGA, HGS, LBM, and FM) assessed close to start of dialysis and outcome. As expected, both male (log rank 32.4, $P<0.0001$) and female (log rank 13.7, $P<0.001$) ESRD patients classified as malnourished (SGA >1) had a significantly higher mortality rate than those classified as well-nourished (Figure 3). In the whole patient group, those with a HGS above the median had a significantly (log rank 7.2, $P<0.01$) better survival rate than those with a HGS below the median. However, when the patient material was divided according to gender, HGS was shown to be an excellent predictor of outcome in males (log rank 23.0, $P<0.0001$) only (Figure 4). No difference (log rank 1.7) in survival rate was seen in the entire patient group when median LBM was used as predictor of outcome. However, when the patients were analysed with regard to gender, a significantly (log rank 7.8, $P<0.01$) lower survival rate was found in males with LBM below median, whereas no significant difference (log rank 0.7) in outcome was detected in females with high or low LBM, respectively. Finally, no differences in outcome were observed in males (log rank 0.6) or females (log rank 1.1) using the median of total FM weight as a predictor of outcome.

The Cox proportional hazard model was used to adjust event-free times for age and co-morbidity (CVD and DM), the presence of inflammation (CRP $\geqslant 10$ mg/l), and five different baseline nutritional parameters (HGS, SGA, S-albumin, LBM, and FM) in the whole patient group as well as in male and female subgroups, respectively (Table 2). In the whole patient group, only elevated CRP ($P<0.05$) and SGA >1 ($P<0.001$) provided additional predictive information on outcome following the correction for age and co-morbidity. Inclusion of mode of treatment

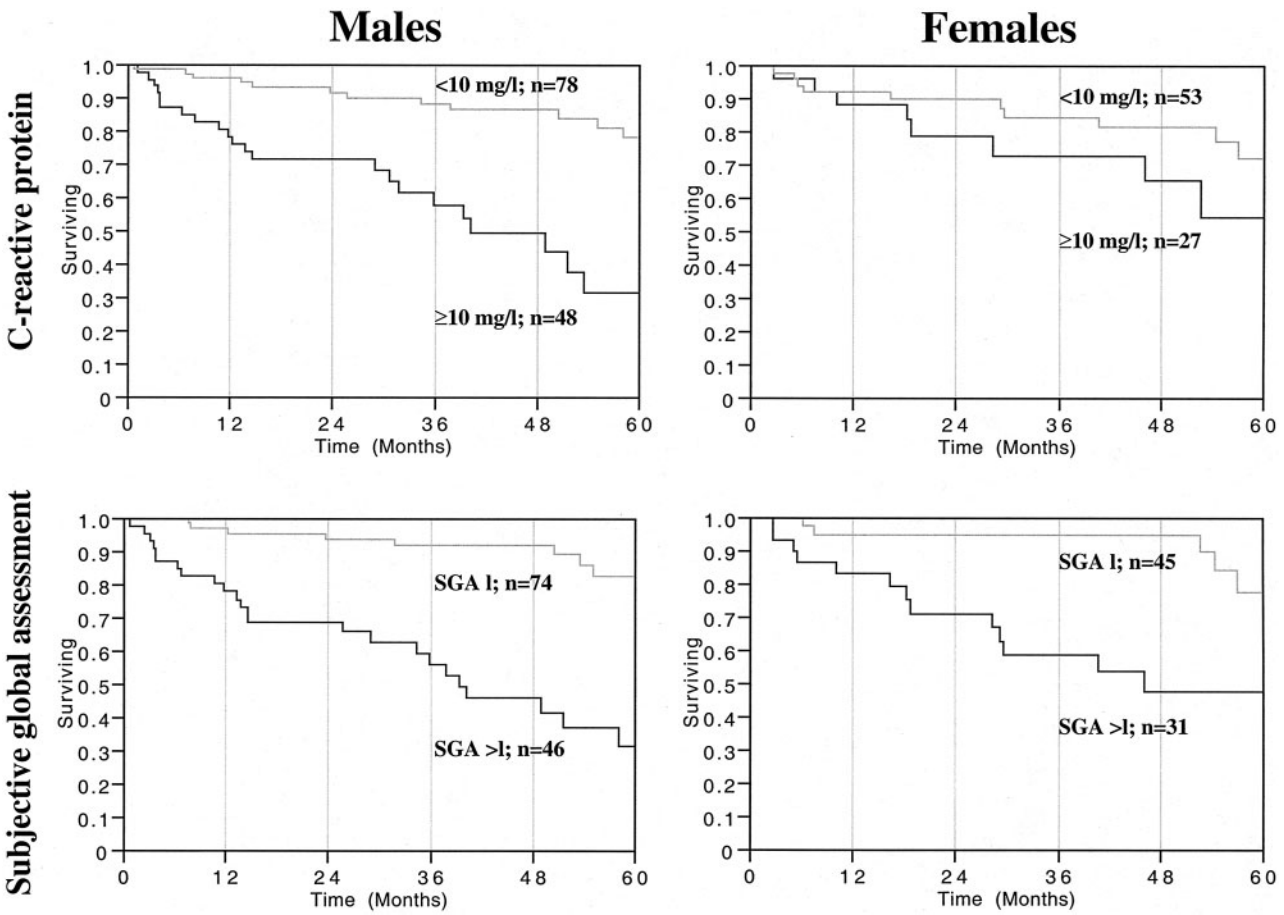

Fig. 3. Survival by Kaplan–Meier in males (left) and females (right) according to the presence of inflammation (log rank 24.3, $P<0.0001$ *vs* log rank 1.7, NS) and SGA (log rank 32.4, $P<0.0001$ *vs* log rank 13.7, $P<0.001$) evaluated at start of RRT.

modality as a potential confounder did not affect the hazard ratios. In males, elevated CRP ($P<0.01$), low HGS ($P<0.01$), SGA >1 ($P<0.01$) and low S-albumin levels ($P<0.05$) at start of RRT predicted outcome following the correction of age and co-morbidity (Table 2). It is notable that in females, only SGA >1 ($P<0.001$) added independent predictive information following correction for age, CVD, and DM (Table 2).

Discussion

The present prospective cohort study confirms that beside age, the presence of CVD and DM [16] are associated with poor outcome in ESRD patients starting RRT. Our data demonstrate that the unadjusted hazard ratio for CVD was 2.64 (95% CI: 1.99–3.56) and for DM 1.56 (95% CI: 1.19–2.04). The results of the present study also show that the unadjusted hazards ratio for the presence of inflammation (CRP >10 mg/l) at start of RRT was 1.83 (95% CI: 1.40–2.41). Following adjustment for age, sex, CVD, and DM, the hazard ratio for CRP $\geqslant 10$ mg/l was still significant 1.36 (95% CI: 1.01–1.83). Thus, overall mortality rate during the observation period was significantly higher in patients with elevated CRP (41% *vs* 18%), which is similar to data previously reported by Zimmermann *et al.* [16]. Inclusion of mode of treatment modality as a potential confounder did not affect the hazard ratios and treatment modality itself did not contribute to poor survival (Figure 1). The results of the present study suggest that important differences between males and females exist with regard to inflammation as a predictor of poor outcome. Thus, whereas elevated CRP was a strong independent risk factor in males, elevated CRP was not associated with poor outcome in females (Table 2). Although the lower number of females in the study (80 *vs* 126 males) could suggest that limited statistical power may explain this finding, the number of included females should be sufficient to observe a difference if inflammation was, indeed, a major risk factor for poor outcome in females. Nevertheless, our finding needs to be confirmed in a larger group of ESRD female patients. However, it is also possible that important differences between the sexes may exist with regard to the atherogenic potential of inflammation. In fact, female sex hormones have been shown to play an important role in maintaining immune function and have been shown to provide a survival advantage against septic challenge [17].

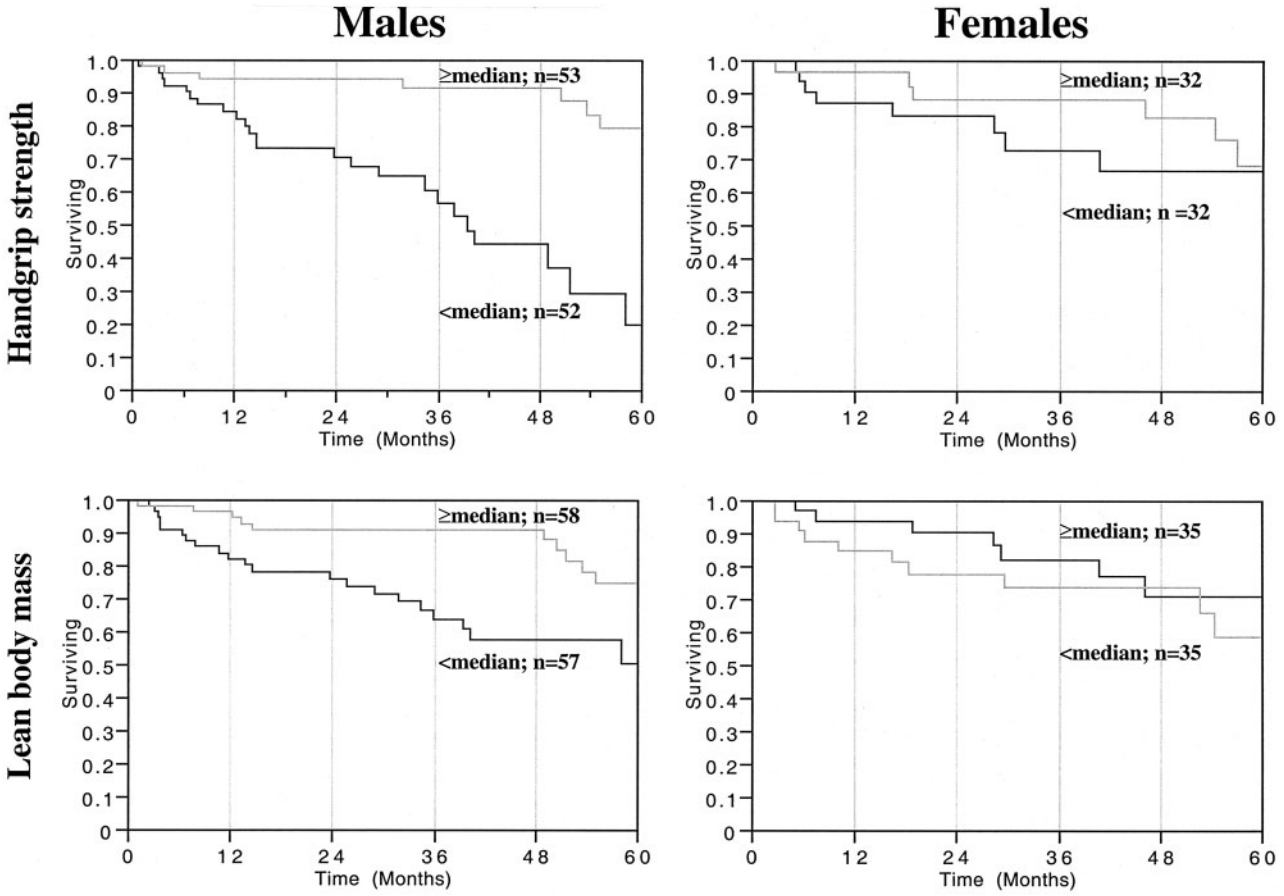

Fig. 4. Survival by Kaplan–Meier in males (left) and females (right) according to HGS (log rank 23.0, $P < 0.0001$ *vs* log rank 1.0, NS) and LBM (log rank 7.8, $P < 0.01$ *vs* log rank 0.7, NS) evaluated at start of RRT.

In the present study, mild to moderate malnutrition, assessed by SGA, was found in 39% of the patients. At least three previous studies have used SGA to assess nutritional status in patients before start of RRT with a prevalence of mild to severe malnutrition ranging from 28% to 55% [5,6,18]. It seems likely that differences in criteria for patient selection may explain the differences observed. Several previous studies have also shown that signs of malnutrition are strong predictors of the clinical outcome in ESRD patients [4,6,18,19]. Malnutrition is usually diagnosed by finding specific changes in various biochemical markers or in anthropometric measurements. The evaluation of nutritional status has previously been based mainly on measurements of biochemical markers, such as S-albumin [20], prealbumin, and transferrin [4,19]. However, since these proteins are affected by inflammation and systemic disease, their use for evaluation of malnutrition has been criticized [10,12]. Obviously, other inexpensive and easily performed parameters are needed to assess nutritional status in ESRD patients. Various nutritional parameters, e.g. anthropometry [2], SGA [6], S-creatinine [4], and total body nitrogen [21], reportedly predict mortality in ESRD patients. Our findings confirm that some of these parameters may predict outcome during dialysis, but show that the statistical power of such associations is dependent on sex. It is notable that neither LBM nor FM independently predicted outcome in males or females in the present study.

Handgrip strength predicts outcome only in males

Handgrip strength has previously been reported to predict mortality and complications in surgical patients [22] and we [10] have found that HGS is an easily performed nutritional parameter in ESRD patients. In the present study, we have shown that HGS is an excellent predictor of outcome in male but not female patients. Interestingly, two different nutritional markers associated with low muscular mass and/or strength (LBM, HGS) seems to be related to poor outcome in males only (Figure 4). On the other hand, SGA, a combined subjective nutritional parameter in which muscular mass is not directly assessed, was shown to be a valid independent predictor of mortality in both sexes. Thus, our findings indicate that sex is an important factor that should be taken into consideration in future studies when the effects of various nutritional interventions are studied in ESRD patients.

Several factors might explain why HGS is associated with poor outcome in males only. First, the construction of the device used to measure HGS

Table 2. Unadjusted and adjusted hazard ratios for overall mortality in patients starting renal replacement therapy.

Variable	Unadjusted hazard ratio (95% CI)	*P* value	Adjusted hazard ratio (95% CI)[a]	*P* value
All patients ($n=206$)				
Age (per year) increase	1.07 (1.04–1.10)	<0.0001	–	–
Sex (male)	1.14 (0.87–1.53)	NS	–	–
Co-morbidity				
CVD	2.64 (1.99–3.56)	<0.0001	–	–
DM	1.56 (1.19–2.04)	<0.01	–	–
Inflammation (CRP ⩾10 mg/l)	1.83 (1.40–2.41)	<0.0001	1.36 (1.01–1.83)	<0.05
Nutritional parameters				
HGS (per kg) increase	0.95 (0.92–0.97)	<0.0001	0.96 (0.93–1.01)	NS
Malnutrition (SGA >1)	2.34 (1.75–3.20)	<0.0001	1.78 (1.31–2.49)	<0.001
S-alb (per g/l) increase	0.95 (0.91–0.98)	<0.01	0.96 (0.93–1.01)	NS
LBM (per kg) increase	0.99 (0.97–1.02)	NS	0.98 (0.93–1.02)	NS
TFM (per kg) increase	0.99 (0.96–1.02)	NS	0.98 (0.95–1.01)	NS
Males ($n=126$)				
Age (per year) increase	1.08 (1.04–1.12)	<0.0001	–	–
Co-morbidity				
CVD	2.54 (1.80–3.70)	<0.0001	–	–
DM	1.59 (1.15–2.20)	<0.01	–	–
Inflammation (CRP ⩾10 mg/l)	2.42 (1.59–3.23)	<0.0001	1.66 (1.15–2.42)	<0.01
Nutritional parameters				
HGS (per kg) increase	0.90 (0.87–0.94)	<0.0001	0.93 (0.89–0.97)	<0.01
Malnutrition (SGA >1)	2.48 (1.74–3.68)	<0.0001	1.69 (1.16–2.56)	<0.01
S-alb (per g/l) increase	0.94 (0.91–0.98)	<0.01	0.95 (0.91–0.99)	<0.05
LBM (per kg) increase	0.94 (0.90–0.98)	<0.01	0.95 (0.89–1.00)	0.06
TFM (per kg) increase	0.99 (0.95–1.03)	NS	0.99 (0.94–1.04)	NS
Females ($n=80$)				
Age (per year) increase	1.05 (1.01–1.10)	<0.05	–	–
Co-morbidity				
CVD	2.82 (1.73–4.80)	<0.0001	–	–
DM	1.43 (0.84–2.30)	NS	–	–
Inflammation (CRP ⩾10 mg/l)	1.36 (0.84–2.17)	NS	1.01 (0.56–1.79)	NS
Nutritional parameters				
HGS (per kg) increase	0.94 (0.80–1.01)	NS	0.97 (0.90–1.04)	NS
Malnutrition (SGA >1)	2.18 (1.34–3.85)	<0.01	2.56 (1.45–4.88)	<0.001
S-alb (per g/l) increase	0.97 (0.90–1.04)	NS	1.03 (0.94–1.13)	NS
LBM (per kg) increase	1.04 (0.97–1.13)	NS	1.02 (0.91–1.11)	NS
TFM (per kg) increase	1.00 (0.90–1.04)	NS	0.98 (0.94–1.02)	NS

S-alb, S-albumin; TFM, total fat mass; NS, not significant.
[a]Adjusted for age, CVD, and DM.

(Harpenden dynamometer) might mean that it is not suitable for most female patients. It is also possible that men are more competitive than women are and, perhaps, try harder to obtain better handgrip results. However, since another indirect measurement of muscular mass, LBM, also showed an association between a reduction in muscular mass and a poor survival in male patients only, this seems unlikely. Third, fewer females than males were studied and the range of HGS values were narrower among females than males. Finally, the risk factor profile may be very different in male and female ESRD patients and the loss of muscular mass might be a much more ominous sign in males. Interestingly, studies in HIV-infected persons have shown that women lose more fat than LBM, but men lose about equal amounts of both [23]. The cause(s) of this dimorphism is not clear but it could be related to the different physiological effects of sex hormones. Clearly, further research in this area is needed.

S-albumin has limited use as a marker of nutritional status

The poor correlations between S-albumin, estimated protein intake and other nutritional factors in the present study indicate that non-nutritional factors, such as co-morbidity, may be more important than nutritional status in determining S-albumin levels at the pre-dialysis stage. Actually, whereas no significant difference in S-albumin levels was found between malnourished and well-nourished ESRD patients, those patients with significant co-morbidity, such as CVD, DM, and inflammation, had significantly lower levels of S-albumin. Thus, our data confirm those previously reported by Struijk *et al.* [13] suggesting that co-morbidity may be more important than malnutrition in determining S-albumin levels in ESRD patients. Indeed, previous studies have shown that S-albumin alone has limited use as an index of nutritional status [8,10] and the present data show

that following correction for the impact of inflammation and age the predictive value of S-albumin on outcome is lost.

Conclusions

The present study confirms that the presence of CVD, DM, and inflammation all predict poor outcome during RRT. Also, poor nutritional status, evaluated by SGA, is an important independent predictor of poor outcome in both males and females. However, important differences as regards to the predictive power of various other nutritional parameters and the presence of inflammation seem to exist between the sexes. Thus, whereas elevated CRP, low S-albumin, and HGS predict outcome in male patients, no predictive effect of these parameters was found in females. Thus, for nutritional evaluation of ESRD patients, we recommend SGA, which is easy to perform and gives independent predictive information in both sexes. Handgrip strength, on the other hand, is of value for nutritional assessment in male ESRD patients only. Our data also suggest that S-albumin seems to be more closely associated to co-morbidity and age than the nutritional status *per se*.

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