The prognostic impact of fluctuating levels of C-reactive protein in Brazilian haemodialysis patients: a prospective study

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Abstract

Background. A single elevated C-reactive protein (CRP) value predicts mortality in haemodialysis (HD) patients, but the relative importance of repeated vs occasional positive systemic inflammatory response findings is not known.

Methods. To assess the influence on survival of occasional inflammation, CRP, serum albumin (S-Alb) and fibrinogen were analysed bimonthly in 180 HD patients (54% male, 49±14 years). Clinically significant inflammation was defined as CRP > 5.1 mg/l, based on the receiver operating characteristic curve for CRP as predictor of death. Based on four consecutive measurements of CRP, patients were assigned into three groups: group 1 (n = 74; 41%), no inflammation (CRP ≤ 5.1 mg/l in all measurements); group 2 (n = 65; 36%), occasional inflammation (1–3 measurements of CRP > 5.1 mg/l); and group 3 (n = 41; 23%), persistent inflammation (all measurements of CRP > 5.1 mg/l). The nutritional status was evaluated by subjective global assessment (SGA) and body mass index (BMI), and the survival (21 months of follow-up) by Kaplan–Meier curve and Cox model.

Results. The median and range of CRP values (mg/l) for group 1, 2 and 3 were: 3.2 (3.2–5.1), 3.6 (3.2–54.9) and 13.8 (5.2–82), respectively (P < 0.001), whereas the prevalence of malnutrition, assessed by SGA and BMI, did not differ significantly among the groups. The survival rate by Kaplan–Meier analysis was significantly different among the groups (χ² = 12.34; P = 0.0004). Patients in group 3 showed the highest mortality (34%; P = 0.001), compared with group 1 (8%) and group 2 (14%; P = 0.01), respectively, whereas there was no significant difference in mortality between groups 1 and 2. Age, CRP, S-Alb level and SGA were independent predictors of mortality.

Conclusion. The patients with a persistent elevation of CRP had a higher mortality rate than the patients with occasional CRP elevation. Thus, persistent, rather than occasional, inflammation is an important predictor of death in HD patients.

Keywords: C-reactive protein; ESRD; haemodialysis; inflammation; malnutrition

Introduction

Despite the rapid improvement in dialysis technology, the annual mortality rate of patients with end-stage renal disease (ESRD) is many fold higher than that of the general population. This difference is mainly due to accelerated atherosclerosis and increased mortality associated with cardiovascular disease (CVD) [1]. The focus on the pathogenic mechanisms of the atherosclerotic process has been changing during the last decade, and interest in the role of inflammation in the atherosclerotic process is expanding [2]. Moreover, 40% of patients undergoing maintenance dialysis suffer from varying degrees of malnutrition, and a poor nutritional status is associated with inflammation, CVD and increased mortality in patients with ESRD [3].

Cross-sectional studies based on a single determination of C-reactive protein (CRP) show that ~30–50% of pre-dialysis, haemodialysis (HD) and peritoneal dialysis (PD) patients have serological evidence of an activated inflammatory response with elevated serum
levels of CRP [2]. However, inflammation may fluctuate over time, and the appearance of clinical events in dialysis patients might be related mainly to persistent rather than to occasional elevations in plasma CRP levels [4,5]. Although it is well documented that CVD mortality is significantly higher in HD patients with a single elevated CRP [6], the consequences, in terms of clinical outcome of fluctuating levels of CRP, have not been established. To test the hypothesis that occasional inflammatory activation has an impact on the survival of ESRD patients, we prospectively measured bimonthly CRP levels in 180 HD patients for 6 months. Their clinical, laboratory and nutritional status were assessed and the patients were then followed for a mean period of 21 months, during which time mortality was recorded.

**Subjects and methods**

**Patients and study design**

All prevalent HD patients in three dialysis centres in Curitiba, in southern Brazil, were initially enrolled in the present study, which consisted of two parts. In the first part (pre-baseline), the patients underwent bimonthly assessments of inflammation for 6 months. At the end of this period, the patients underwent a clinical and nutritional assessment (baseline investigation). In the second follow-up phase of the study, mortality was recorded. To be included in the second part of the study, the patients were required to have completed four consecutive measurements of CRP during the preceding 6 months. The exclusion criteria were presence of a known chronic inflammatory disease or active infection during the initial 6 months of the study. Among the 264 patients who were initially enrolled in the study, 180 (68%) patients (97 men and 83 women) met the inclusion criteria. The clinical and baseline data are shown in Table 1. The median age was 48 years (range 16–89). The causes of renal failure were: chronic glomerulonephritis (n = 63; 36%), hypertensive nephrosclerosis (n = 47; 26%), diabetic nephropathy (n = 17; 9%) and other causes (n = 53; 29%). All patients were haemodialysed 3–4 h three times weekly with modified cellulosic membranes (low flux dialysers of cellulose acetate or derivatized cellulose). The vast majority of the patients had native AV fistula and only 5% had vascular grafts. Medications included human recombinant erythropoietin, iron saccharate, calcium-based phosphate binders, oral active vitamin D and angiotensin-converting enzyme inhibitors, and anti-inflammatory drugs such as aspirin were used as antplatelet aggregation therapy only in a few patients. The Ethics Committee of Hospital Evangélico de Curitiba approved the study protocol, and informed consent was obtained from all patients.

Clinically significant inflammation was defined as CRP >5.1 mg/l, based on the receiver operating characteristics (ROC) curve, which showed a threshold value of CRP >5.1 mg/l as a predictor of death (Figure 1). According to the results of the four consecutive CRP measurements during the pre-baseline period, and using the ROC cut-off value for CRP, the patients were allocated into three groups: group 1 (n = 74), no significant inflammation (all four CRP values ≤5.1 mg/l); group 2 (n = 65), fluctuating inflammation (at least one CRP value >5.1 mg/l); and group 3 (n = 41), persistent inflammation (all four CRP values >5.1 mg/l).

**Laboratory methods**

Venous blood samples were taken prior to the initiation of the HD session and were stored on ice (4°C) and then centrifuged within 60 min after collection. Samples were thereafter stored at –20°C until analysis. Serum determinations of CRP (nephelometric immunoassay; only values ≥3.2 mg/l were reported), serum albumin (S-Alb) (bromcresol green method) and fibrinogen (measured by the thrombin time method, with a blood sample anticoagulated with 3.8% sodium citrate) were performed bimonthly during the 6 months prior to the follow-up period. Haemoglobin and serum urea, determined by routine methods, and dialysis adequacy (Kt/V) as assessed by the Daugirdas equation [7], were analysed at baseline.

**Nutritional evaluation**

The subjective global assessment (SGA) and body mass index (BMI; kg/m²) were used to evaluate the nutritional status at baseline. SGA, which was performed in 159 out of

**Table 1.** Clinical and laboratory data in 180 haemodialysis patients at the end of the baseline period

| Age (years) | 49 ± 14 |
| Males (%)   | 55     |
| Time on HD (months) | 59 ± 37 |
| CRP (mg/l) | 3.6 (3.2–82) |
| S-Alb (g/dl) | 3.5 ± 0.3 |
| BMI (kg/m²) | 23.5 ± 4.6 |
| Fibrinogen (mg/dl) | 500 ± 140 |
| Kt/V urea | 1.3 ± 0.2 |
| Malnutrition (SGA B and C) (%) | 62 |
| Diabetes mellitus (%) | 9 |

*aValues are expressed as means ± SD; bValues are expressed as median and range; *n = 129; *n = 159.

**Fig. 1.** Receiver operating characteristics (ROC) curve for CRP as a predictor of death.
180 patients, included six subjective assessments; three assessments were based on the patient’s history of weight loss, incidence of anorexia and incidence of vomiting, and three were based on the dietitian’s grading of muscle wasting, presence of oedema and loss of subcutaneous fat. On the basis of these assessments, each patient was given a ranking that reflected the nutritional status as follows: A = normal nutritional status, B = mild to moderate malnutrition and C = severe malnutrition [8]. BMI was calculated from height and weight, and according to the results the patients were distributed in three groups: low BMI (BMI \( \leq 20 \text{ kg/m}^2 \)), normal BMI (BMI between 20 and 25 kg/m\(^2\)) and high BMI (BMI \( \geq 25 \text{ kg/m}^2 \)) [9]. The baseline SGA and BMI were determined at the beginning of the follow-up period and by the same experienced dietitian.

**Follow-up**

After the baseline investigation, the patients were followed prospectively for the subsequent 21 months to determine their clinical outcome. Survival was recorded from the end of the pre-baseline period of sample collection (from September 2000 to May 2002), until death \((n = 27)\) or censoring for transplantation \((n = 13)\).

**Statistical analysis**

We expressed normally distributed variable as the mean± SD and skewed distributed variable as median and range. A P-value <0.05 was considered significant. A comparison between two groups was performed using the Student t-test for normally distributed variables, whereas the Mann–Whitney’s U-test was used for skewed distributed variables. Comparisons between three groups were performed using the analysis of variance (ANOVA) test. The analysis of categorical variables was made by the analysis of contingency tables. For non-normally distributed variables, correlations were performed with the Spearman rank test. The Kaplan–Meier test was used for analysis of survival. Cox proportional hazard analysis was used to assess independent predictors of survival. The cut-off point for CRP, as predictor of clinical outcome, reached a sensitivity and specificity of 63 and 47.3%, respectively, according to the ROC curve (Figure 1).

The area under the ROC curve was 0.696, standard error \(0.058\), 95% confidence interval 0.564–0.795 and \(P = 0.001\). We performed all statistical analyses using NCSS 2001 and PASS 2002 (J. Hintze NCSS and PASS statistical system Kaysville, UT).

**Results**

**Clinical data**

The clinical data and serum concentrations of CRP, S-Alb and fibrinogen for the 180 patients are summarized in Table 1. Malnutrition, defined by SGA (ranking B to C), was present in 99 (62%) patients of the 159 patients investigated; 85 (53%) patients were mildly malnourished and 14 (8%) patients were severely malnourished. The mean BMI was 23.5± 4.6 kg/m\(^2\) for the whole studied population. There were 43% of the patients with a BMI between 20 and 25 kg/m\(^2\), 33% with values >25 kg/m\(^2\) and 24% with BMI <20 kg/m\(^2\). The median and range and mean± SD values of CRP, S-Alb and fibrinogen at the baseline investigation were, respectively, 3.6 mg/l (range 3.2–82), 3.5±0.3 g/dl and 500±140 mg/dl. An increased CRP level (defined as CRP >5.1 mg/l) was found in 66 (37%) patients at the first available measurement during the pre-baseline period, and 106 (59%) patients had an elevated CRP level at least once during the pre-baseline 6 months period, and in 37% of the patients the CRP level was elevated in all four measurements. Among the 66 patients who had an elevated initial CRP, 45 (68%) persisted with CRP >5.1 mg/l at the final measurement. On the other hand, only 28 out of 114 patients who presented with a low initial CRP had an elevated final measurement. In addition, after excluding patients with an identifiable cause of inflammation (episodes of acute infection and the presence of chronic inflammatory diseases) at the pre-baseline period, 45 (24%) patients had signs of either inflammation or malnutrition.

At baseline, there was a correlation between CRP and fibrinogen \((r = 0.43; P < 0.001)\), but, unexpectedly, not between CRP and S-Alb \((P = 0.15)\), fibrinogen and S-Alb \((P = 0.04; P = 0.6)\) or CRP and age \((P = 0.08; P = 0.28)\). Patients classified as malnourished by SGA were significantly older \((51\pm13 \text{ vs } 45\pm14 \text{ years}; P = 0.02)\) compared with well-nourished patients. Otherwise the malnourished patients did not differ significantly from the well-nourished patients with regard to a variety of biochemical parameters including S-Alb \((3.4\pm0.3 \text{ vs } 3.5\pm0.3 \text{ g/dl}; P = 0.2)\), fibrinogen \((510\pm130 \text{ vs } 480\pm120 \text{ mg/dl}; P = 0.2)\) and CRP \((3.7\text{ (3.2–82)} \text{ vs } 3.6\text{ (3.2–15.6) mg/l}; P = 0.48)\), respectively (Table 2).

According to the BMI, the prevalence of malnutrition was 24% in the entire cohort. Although no significant differences in S-Alb, CRP, fibrinogen, SGA and gender could be observed between the groups, patients with lower BMI were significantly younger and had a higher \(Kt/V\) compared with the other two groups (Table 3). Furthermore, a significant

**Table 2. Clinical and laboratory comparison according to baseline nutritional status in 159 patients**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Malnourished ((n = 99))</th>
<th>Well nourished ((n = 60))</th>
<th>(P)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males (%)</td>
<td>51</td>
<td>49</td>
<td>0.4</td>
</tr>
<tr>
<td>Age (years)(^a)</td>
<td>51±13</td>
<td>45±14</td>
<td>0.02</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>13</td>
<td>8</td>
<td>0.2</td>
</tr>
<tr>
<td>CRP (mg/l)(^b)</td>
<td>3.7 (3.2–82)</td>
<td>7</td>
<td>0.5</td>
</tr>
<tr>
<td>BMI (kg/m(^2))(^c)</td>
<td>23.7±3.9</td>
<td>23.4±4.7</td>
<td>0.48</td>
</tr>
<tr>
<td>S-Alb (g/dl)(^d)</td>
<td>3.4±0.3</td>
<td>3.5±0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)(^b)</td>
<td>510±130</td>
<td>480±120</td>
<td>0.2</td>
</tr>
<tr>
<td>(Kt/V)(^e)</td>
<td>1.3±0.2</td>
<td>1.3±0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Time on HD (months)(^f)</td>
<td>58±41</td>
<td>60±32</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Malnutrition was defined as SGA category B or C. 
\(^a\)Values at baseline are expressed as mean± SD; \(^b\)values at baseline are expressed as median and range; \(^c\)\(n = 129\).
correlation was found between BMI and age ($r = 0.22$; $P = 0.002$), BMI and $Kt/V$ ($r = -0.22$; $P = 0.01$) and BMI and time on HD ($r = 0.15$; $P = 0.04$). On the other hand, there was no significant correlation between BMI and inflammatory parameters such as CRP, S-Alb and fibrinogen.

Comparisons between the three CRP groups

The clinical characteristics of the three groups are given in Table 4. The individual values of CRP in group 2 are presented in Figure 2. The 65 patients in group 2 had an elevated CRP at one (31 patients), two (25 patients) or three (11 patients) determinations. Whereas S-Alb levels did not differ significantly among the three groups, patients in group 3 had significantly ($P < 0.001$) higher levels of fibrinogen ($580 \pm 130$ mg/dl) compared with patients in group 1 ($440 \pm 120$ mg/dl) and group 2 ($520 \pm 130$ mg/dl). Surprisingly, neither SGA nor BMI differ significantly among the three groups. Although patients in group 3 had lower levels of $Kt/V$ ($1.2 \pm 0.2$) compared with patients in group 1 ($1.3 \pm 0.2$) and group 2 ($1.3 \pm 0.2$), this difference did not attain full statistical significance ($P = 0.06$).
Persistent inflammatory activity and clinical outcome

Table 5. Cox proportional hazards multivariate analysis of factors predicting mortality in 159 subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Adjusted hazard ratios (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per year)</td>
<td>1.05 (1.02–1.09)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Gender (M vs F)</td>
<td>0.95 (0.98–2.28)</td>
<td>0.91</td>
</tr>
<tr>
<td>Malnutrition (SGA B and C vs A)</td>
<td>0.29 (0.07–0.60)</td>
<td>0.0007</td>
</tr>
<tr>
<td>S-Alb (per g/dl increase)</td>
<td>0.22 (0.07–0.63)</td>
<td>0.005</td>
</tr>
<tr>
<td>CRP (per mg/l increase)</td>
<td>1.03 (1.00–1.06)</td>
<td>0.01</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>1.00 (0.99–1.00)</td>
<td>0.59</td>
</tr>
<tr>
<td>BMI (&lt; 20 kg/m² vs ≥ 20 kg/m²)</td>
<td>0.74 (0.37–1.42)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

SGA, BMI, S-Alb, fibrinogen and CRP were assessed at baseline.

Survival analysis

During the follow-up, 27 patients died (8, 14 and 34% for groups 1, 2 and 3, respectively). The causes of death were CVD (52%), infection (30%) or other causes (18%). The survival in the patients in groups 1, 2 and 3 is shown in Figure 3. According to the Kaplan–Meier analysis for the overall population, the survival rate was significantly different among the groups ($\chi^2 = 12.34; P = 0.0004$). When analysed separately, there were no significant differences in mortality between group 1 and 2 ($\chi^2 = 0.67; P = 0.5$), but significantly higher mortality in group 3 compared with group 2 ($\chi^2 = 7.1; P = 0.01$) and between group 3 and group 1 ($\chi^2 = 11.97; P = 0.0007$). Moreover, it should be noted that whereas the Kaplan–Meier survival analysis showed no impact of low BMI on survival ($\chi^2 = 1.73; P = 0.42$), patients classified as malnourished by SGA had a marked increase in mortality ($\chi^2 = 15.24; P < 0.001$).

The Cox proportional hazard model was applied to the 159 patients who had their SGA evaluated, to adjust event-free times for age, SGA, CRP, S-Alb, fibrinogen and gender (Table 5). The Cox analysis showed that SGA, S-Alb, age and CRP were associated with clinical outcome. On the other hand, gender, BMI and fibrinogen were not associated with clinical outcome. Compared with survivors, non-survivors had a higher median level of CRP [6.2 (3.2–82) mg/l vs 3.2 (3.2–28.30) mg/l], lower levels of S-Alb (3.3 ± 0.5 vs 3.5 ± 0.3 g/dl) and were older (57 ± 14 vs 48 ± 14 years), respectively. According to SGA, almost all non-survivors were malnourished (96%), whereas no significant difference in BMI was found between non-survivors (22.9 ± 3.7 kg/m²) and survivors (23.6 ± 4.7 kg/m²) ($P = 0.7$).

Discussion

The main finding of the present study was that the 23% of HD patients who had persistently elevated plasma levels of CRP had a poorer clinical outcome compared with HD patients who had occasional elevations (36% of patients) or low plasma levels (41% of patients) of CRP. Thus, persistent rather than occasional inflammation was a better predictor of death in this study. In addition, malnutrition, defined by SGA, was found in 62% of the patients, whereas only 24% had the same classification by BMI. Furthermore, only SGA, not BMI, predicted mortality. However, in contrast to several previous studies, from Europe and North America, the correlations between inflammatory markers and nutritional status were weak, suggesting that inflammation was not a strong determinant of nutritional status in this South American cohort.

The high prevalence of inflammation in this Brazilian HD cohort confirms that inflammation is an important clinical feature in ESRD patients, regardless of the geographical origin.

It is now well recognized that there are strong relationships between malnutrition, inflammation and CVD in ESRD patients [2,6,10,11]. The malnutrition, inflammation and atherosclerosis (MIA) syndrome is associated with a high mortality, and in this syndrome, inflammation appears to have a crucial role [2]. Although the origin of inflammation in ESRD patients is often unclear, chronic bacterial or viral infection, loss of residual renal function, uraemia per se and, in HD patients, the influence of the dialysis procedure are thought to be important factors [12]. In the present study, we found that 59% of our patients, who had no signs of clinically apparent infection had an elevated level of CRP (>5.1 mg/l) on one or more occasions during the initial 6 months of the pre-baseline period, confirming that ESRD is a chronic inflammatory state.

When comparing the present data with previous European and North American studies, several important differences should be considered. First, in our study, chronic glomerulonephritis and hypertensive nephrosclerosis were the most common causes of ESRD, which is in agreement with data from the Latin American Registry [13]. Secondly, in contrast to North American and European studies in which the prevalence of diabetic nephropathy in HD is higher [14], the prevalence of diabetic nephropathy was only ~9% in the present study. This might be explained by the fact that most diabetic patients in our clinic are being treated by PD. Another important fact to consider is that the mean age was considerably lower compared with European and North American dialysis patients [6,11].

Most of the studies analysing the inflammatory profile and malnutrition in ESRD patients are from industrialized Western and Asian countries, whereas in other countries the real estimation of the MIA syndrome remains unclear [15]. The prevalence of malnutrition (based on SGA) in our population (62%) was similar to that reported previously from Sweden [11], but is higher than the prevalence in other studies [16], especially in Asian patients in whom malnutrition as well as inflammation may be less common. Noh et al. [17] found that 12% of 106 patients on PD in Korea had signs of inflammation, and even in this group the prevalence of malnutrition was only 30.8%. These divergent findings might be explained by differences in socio-economic, nutritional
Inflammation and mortality

The acute phase response usually varies over time in dialysis patients, suggesting that a transitory process, such as infections, is often responsible for activation of the inflammatory response [19]. When we analysed the variation of CRP levels in our patients, we could identify a group of patients in whom the levels of CRP fluctuated between normal and abnormal values (group 2). From a clinical point of view, it is important to understand the implications of the inflammatory response of patients in group 2 who sometimes presented with CRP levels within the limits of normality. These patients had, according to the Kaplan–Meier analysis, a better survival rate compared with the persistently inflamed patients in group 3.

One possibility that might explain the poor survival in group 3 is that this group may have had more co-morbid conditions compared with the other two groups; in fact, they had higher levels of fibrinogen, a higher prevalence of malnutrition and were older compared with the other two groups. We have shown previously that the mortality rate increases progressively with an increasing number of risk factors (malnutrition, inflammation and CVD), being as high as 75% after 3 years in patients who have all these three risk factors [11]. In this study, we could confirm that age, S-Alb, CRP and malnutrition were independent predictors of mortality. Similarly, Zimmermann et al. [10] and Yeun et al. [6] found that CRP and age were the most important factors in predicting CVD mortality among European and North American HD patients. The difference in mortality between group 2 and group 3 in the present study could also be related to the fact that patients from group 2 were younger and presented with on average lower levels of CRP, reflecting a lower degree of persistent inflammatory activity. It is notable that patients from group 3 also, presented with persistently higher levels of CRP during the follow-up period (data not shown), thus demonstrating a continual pattern of a systemic inflammatory response.

This study confirms strong correlations between the acute phase proteins, CRP and fibrinogen [2,6,10]. Fibrinogen levels are elevated in patients with chronic renal failure [20], and inflammation of coronary artery plaques is predicted by high values of CRP and fibrinogen [6]. However, surprisingly, S-Alb levels were not associated with CRP when all 180 patients were analysed in the present study. Nevertheless, a strong negative correlation was found when the analyses were limited to the non-survival group (data not shown), suggesting that hypoalbuminaemia associated with systemic inflammation was a marker for mortality in this cohort of HD patients.

Limitations of the study

Several shortcomings of the present study should be considered. First, in our nutritional evaluation, we relied on SGA. Although the National Kidney Foundation Dialysis Outcome Quality Initiative (DOQI) recommends the use of SGA in its most recent update for the evaluation of protein-energy nutritional status [21], a single determination of SGA cannot take into account any variation of the nutritional state that occurred over time. Secondly, the lack of assessment of CVD as a predictor of clinical outcome is another relevant concern. In the present study, as a complete cardiovascular evaluation through invasive or non-invasive investigations was not available in most patients, we did not include an analysis of CVD based on clinical findings. Thirdly, although all patients with known active infection were excluded from the study during the pre-baseline period, subclinical infectious episodes can still not be ruled out as causing the bursts of inflammation in group 2, especially in patients with only one elevated measurement of CRP. The resolution of the infectious process could bring the levels of CRP back to normal, resulting in no harmful effect on clinical outcome. Fourthly, a not high sensitivity CRP test was used, which could have had some influence on the threshold value of 5.1 mg/l used to define clinically significant inflammation. Finally, the inclusion criteria of four consecutive assessments during the 6-month baseline period implying a positive selection of the survivors during this period is another limitation of this study.

In summary, in this cohort of Brazilian HD patients, inflammation and malnutrition were common complications that predicted survival, but did not correlate with each other, suggesting that many of the malnourished patients had malnutrition type 1, i.e. not associated with inflammation, but due to a poor nutritional intake [3]. CRP and S-Alb (single baseline determinations) as well as the presence of malnutrition (detected by SGA but not by BMI) and advanced age were independent and strong predictors of mortality. In the longitudinal part of the study, there were two characteristic groups of patients with elevated levels of CRP: one group with fluctuating levels and another one with persistent inflammatory activity. The patients with
a persistent elevation of CRP had a higher mortality rate than the patients with occasional CRP elevation; in fact, the mortality in the latter group did not differ significantly from the mortality in the non-inflamed patients. Thus, persistent, rather than occasional, inflammation is an important predictor of death in HD patients. Further studies are needed to better understand the underlying cause(s) of a persistent inflammatory response in ESRD patients demonstrating no clinical signs of ongoing infection or inflammatory disease.

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