The predictive value of anthropometric parameters on mortality in haemodialysis patients

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Abstract

Background. Since protein-calorie malnutrition is a common factor influencing morbidity and mortality of haemodialysis patients, assessing their nutritional status is important. The aim of this study was to investigate the predictive value of anthropometric parameters on mortality and their interrelationship.

Methods. The study included a cohort of 242 patients. The analysis involved baseline data obtained during the first calendar year after the patients entered the study (1994–2001) and repeated measurements for up to 132 months of follow-up (until 2004). Anthropometric measurements were made during the winter season and included skinfolds, mid-arm circumference (MAC), body height and weight. The percentage of body fat (%fat) was calculated from triceps (TSF), biceps, subscapular and suprailiac skinfolds (Disease Outcomes Quality Initiative (DOQI) guidelines) and mid-arm muscle circumference (MAMC) from MAC and TSF. Body mass index (BMI), Kt/V, normalized protein catabolic rate (NPCR) and cardiovascular co-morbidity were also determined and laboratory analyses undertaken.

Results. Strong correlations were found among the anthropometric parameters. Extended Cox regression analysis selected %fat, MAC, MAMC and TSF in addition to age, ischaemic heart disease, congestive heart failure, Kt/V, haemoglobin, creatinine, albumin and NPCR as potential predictors of mortality. The same anthropometric parameters were found to be independent mortality predictors in corresponding models. The most predictive anthropometric factor was MAC. BMI was not a risk factor.

Conclusion. Percentage of body fat, MAC, MAMC and TSF were independent predictors of mortality of haemodialysis patients, and MAC was the most predictive one.

Keywords: anthropometry; cohort study; haemodialysis; nutrition; survival analysis

Introduction

Assessing the nutritional status of haemodialysis patients is important because protein-calorie malnutrition is a common factor influencing morbidity and mortality in this group of patients [1–3]. Many methods are available for the assessment of nutritional status of haemodialysis patients [4–6], but albumin concentration and body mass index (BMI) are most frequently employed. On the other hand, the use of other anthropometric parameters is rare and usually involves percentage of body fat (%fat), although more simple anthropometric measurements such as mid-arm circumference, triceps skinfold or mid-arm muscle circumference are also available [6,7]. The aim of the present study was to investigate mortality predictive value of triceps skin fold, mid-arm circumference, mid-arm muscle circumference and percentage of body fat in haemodialysis patients.

Materials and methods

This post hoc analysis of an observational study included a cohort of 242 patients (129 men) on maintenance haemodialysis in the Dialysis Unit of the Clinical Center of Serbia [8]. The design of the study was approved by the Ethics Committee of the Clinical Center.

All patients were monitored until their death (124 patients), kidney transplantation (9 patients), departure from the centre (22 patients), leaving the study (6 patients) or its end on 31 December 2004 (38 men and 43 women).

Baseline measurements were made during the first calendar year the patients entered the study (1 January to 31 December) and involved clinical, anthropometrical and monthly laboratory examinations. After that, the patients were monitored yearly in the same manner. Anthropometric measurements were made by the same investigator every February until the study finished except for 2003, when they could not be done due to technical problems.

The patients were dialysed three times per week for 3–5 h using bicarbonate solutions. The dialysers were never reused. The patients were given a standard diet for haemodialysis patients [9] that did not change during the observation period.
Pre-dialysis blood pressure was measured at the beginning of every dialysis session. Pre-dialysis mean arterial pressure (MAP) was calculated from the formula [MAP = diastolic + (systolic − diastolic)/3]. Patients with a history or signs of ischaemic heart disease and congestive heart failure were considered to have this co-morbidity.

The %fat was determined from the sum of triceps (TSF), biceps, suprailiai and subscapular skinfolds, as recommended by the Disease Outcomes Quality Initiative (DOQI) Clinical Practice Guidelines [10]. Normal intervals for %fat were 12–20% for men and 20–30% for women [11]. Mid-arm muscle circumference (MAMC) was calculated from mid-arm circumference (MAC) using the formula [MAMC (cm) = MAC (cm) − 0.314 * TSF (mm)]. Normal values for TSF, MAC and MAMC were selected as fifth percentile values from tables for upper-arm anthropometry [10,12].

Normalized protein catabolic rate (NPCR) was calculated by variable-volume single-pool urea kinetic modelling from two urea blood samples [13]. Kt/V was obtained using the second-generation Daugirdas formula [14].

\[ Kt/V = -\ln(R - 0.008*t) + (4-3.5R)*UF/W \]

where \( R \) = post-dialysis/pre-dialysis blood urea nitrogen, \( t \) = dialysis hours, \( UF \) = pre-post-dialysis weight change and \( W \) = post-dialysis weight.

Statistical methods

Predictor variables used in the Cox regression were derived from: (i) repeated measurements in the whole observation period; (ii) data in the baseline period and (iii) data from patients at entry to the study.

(i) MAC, MAMC, TSF, %fat and BMI were determined from the once-a-year anthropometric measurements and recorded in a set of variables for baseline period and for every year of follow-up.

Mean values of the pre-dialysis laboratory parameters (albumin, haemoglobin, urea, creatinine, calcium and phosphorus), white blood cells (WBC), Kt/V, NPCR and MAP were calculated for each patient using the values obtained monthly during the 12-month baseline period and every year of follow-up. Separate predictor (continuous) variables were constructed for each parameter for the baseline period and for every year of follow-up. Because the WBC time-varying covariate was not proportional, a new set of binary variables for 11-year period was created. Values for WBC less than 10 × 10⁹/L were coded as 1 and other as 2.

(ii) Co-morbidity was determined during the baseline period, and single binary predictor variables were used for ischaemic heart disease and for congestive heart failure.

(iii) The following predictor variables were noted when patients entered the study: age (years), gender (male/female) and dialysis duration (months). All binary variables were coded as 0/1 if different values were not declared.

Graphic analysis was made to test for agreement between TSF, MAC, MAMC and %fat. Values for %fat were sorted, and areas of low, normal and high levels were drawn on graphs. After that, areas describing low levels of TSF were responsible for end-stage renal disease in one-fifth of the patients.

Laboratory and clinical data in the baseline period are presented in Table 2. Unfortunately Kt/V was below the value recommended by DOQI in more than half of the patients.

Table 4 presents the 5th and 95th percentile values for TSF, MAC and MAMC in the examined patients as well as the normal percentile values reported by Bishop et al. [12]. All parameters in patients were lower than normal values, and the greatest differences between patient and normal values were found for TSF in women and MAC in men.

Graphical analysis revealed good agreement between TSF and %fat in men (Figure 1). However, many women had TSF less than the normal fifth percentile values and at the same time normal %fat. Closer agreement was achieved when the lower level for men was set at 5.0 mm and for women at 6.8 mm (instead of 4.5 and 11 mm). Figure 1 shows that there was marked disagreement between MAMC and %fat. Many men had less than normal fifth percentile values for MAMC and normal or even high %fat. It is hard to determine a cut point value for MAMC that corresponds to normal values for %fat because of large disagreement between them. The graphical relation between MAC and %fat (Figure 1) was somewhat between those for TSF and MAMC. Better agreement was achieved when the lower level was set at 22.5 cm for men and 20.5 cm for women (instead 26.4 and 23.2 cm, respectively). The relationship between MAMC and creatinine is shown in Figure 1 and revealed disagreement similar to that between MAMC and %fat.

There was close correlation among the anthropometric parameters, so these parameters were collinear as well as Kt/V and NPCR (Pearson, \( r > 0.5 \), \( P < 0.01 \)).

In the observation period, 124 patients died. Causes of death are presented in Table 5. A cardiovascular cause of death was registered in 29.8%. Nineteen (15.3%) patients became critically ill and died in the hospital, but 24 (19.4%) patients died at home, and the cause of death has remained unknown.

Kaplan–Meier curves in relation to the nutritional parameters measured in the baseline period are shown in Figure 2. In general, patients in the second tertiles survived the longest over the 11-year observation period, while the first tertile had the shortest survival. Curves for %fat and
TSF were similar as well as for MAC and MAMC. However, all the curves had similar patterns for the first 5 years of the observation period, where third-tertile patients survived as long or even longer than second-tertile ones. After that period, third-tertile patients survived less well and similarly to those in the first tertile. The log-rank test revealed significant differences only for MAC and MAMC (P < 0.05), but when %fat and TSF were tested for the first 5 years of the observation period, near-significant values were obtained, and differences in survival between patients in the first and other two tertiles were significant (P < 0.05). It appeared that muscle mass was more important for patient survival than body fat in the baseline period.

Potential predictors of all-cause death were selected using the univariate extended Cox proportional hazard model (P < 0.10; Table 6). Among anthropometric parameters, %fat, TSF, MAMC and MAC were selected for further analysis but not BMI. Because Kt/V was collinear with NPCR, only the latter was included in multivariate analyses for patients who died from cardiac and cerebrovascular causes. The results of multivariate analysis are presented in Table 7. In every model, diabetes, age, WBC binary, albumin, NPCR and MAC were independent variables together with anthropometric variables. Five models were formed to test the individual predictive power of each anthropometric variable and all anthropometric variables using multivariate extended Cox regression.

The results of multivariate analysis are presented in Table 7. In every model, diabetes, age, WBC binary, albumin and NPCR were independent variables together with anthropometric variables. All tested anthropometric variables had independent predictive power (%fat, MAC, MAMC, TSF). When all anthropometric variables were tested together, MAC was the parameter with the most predictive power. Proportional hazard analysis indicated an average 8.0% reduction in MAC risk, adjusting for age and other factors. Increases in anthropometric parameters reduced the all-cause mortality risk.

Predictors of some causes of death were also analysed. The power of this subgroup analysis is less than the previous all-cause death analysis, but it is still reliable. Survival analysis for patients who died from cardiac and cerebrovascular diseases revealed age, hypertension aetiology, ischaemic heart disease, congestive heart failure, haemoglobin, creatinine, albumin, NPCR and anthropometric variables. Five models were formed to test the individual predictive power of each anthropometric variable and all anthropometric variables using multivariate extended Cox regression.

Cox modelling. Potential risk factors were: underlying kidney disease (diabetes, hypertension and glomerulonephritis), age, WBC binary, ischaemic heart disease, congestive heart failure, haemoglobin, creatinine, albumin, NPCR and anthropometric variables. Five models were formed to test the individual predictive power of each anthropometric variable and all anthropometric variables using multivariate extended Cox regression.

All variables were expressed as mean (SD) and tested as time-dependent covariates for the whole observation period.

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When a subgroup of critically ill patients was analysed, potential predictors of death were: age, diabetes aetiology, ischaemic heart disease, congestive heart failure and low values of %fat, TSF, $Kt/V$, NPCR, albumin, creatinine, urea, haemoglobin and calcium. Independent predictors of death were age, diabetes aetiology and albumin. The number of patients was 127, among whom 19 died.

Analysis of sepsis as a cause of death revealed age, high WBC and low values of Kt/V, albumin, creatinine, NPCR and calcium as potential predictors of death. Albumin and WBC binary were independent predictors of death in multivariate analysis. There were 129 patients, and the number of deaths was 13.

Subgroup analysis of malignancy as a cause of death showed age, diabetes aetiology, congestive heart failure, high WBC, low values of Kt/V, albumin, haemoglobin and calcium as potential predictors in univariate analysis. Multivariate analysis revealed age, albumin, WBC and

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**Fig. 1.** Relationship between TSF, MAMC, MAC and %fat as well as MAMC and creatinine: A, area of low %fat or <5th percentile of creatinine; B, area of normal %fat or 5th to 95th percentile of creatinine; C, area of high %fat or >95th percentile of creatinine; D, area of low values of TSF, MAC and MAMC.
calcium as independent predictors of death. The number of patients was 118, and the number of deaths was 11.

Discussion

The present post hoc analysis of data obtained in an 11-year observational study explores the predictive value of different anthropometric parameters. TSF, MAC, MAMC and %fat were independent predictors of death of haemodialysis patients, but MAC was the most predictive parameter. Increasing anthropometric parameters reduced the mortality risk of the patients. BMI was not a predictor of patient mortality. All anthropometric parameters were mutually highly correlated. The closest agreement was found between TSF and %fat, while the association of both MAC and MAMC with %fat was poor.

The most specific nutritional methods of assessment for haemodialysis patients in our opinion are those that measure %fat (or fat-free mass) because the main function of body fat is to provide an energy reserve. In addition, although the overall muscle mass allows physical activity, most haemodialysis patients are not very active physically, so muscle mass mainly represents nutritional status. However, in the evaluation of nutritional status of haemodialysis patients, the most frequently used nutritional parameters are BMI and albumin concentration because they are simple to measure. On the other hand, neither BMI nor albumin is a specific enough nutritional parameter for haemodialysis patients. It is well known that BMI depends on body frame size and hydration status.

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Number</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac arrest/sudden cardiac death</td>
<td>21</td>
<td>16.9</td>
</tr>
<tr>
<td>Cerebrovascular accidents (CVA)</td>
<td>16</td>
<td>12.9</td>
</tr>
<tr>
<td>Neurologic (except CVA)</td>
<td>6</td>
<td>4.8</td>
</tr>
<tr>
<td>Septicaemia</td>
<td>13</td>
<td>10.5</td>
</tr>
<tr>
<td>Malignant neoplasms</td>
<td>11</td>
<td>8.9</td>
</tr>
<tr>
<td>Gastrointestinal haemorrhage</td>
<td>4</td>
<td>3.2</td>
</tr>
<tr>
<td>Chronic liver disease, cirrhosis</td>
<td>4</td>
<td>3.2</td>
</tr>
<tr>
<td>Critically ill and cachectic (except septicaemia, malignancy and cirrhosis)</td>
<td>19</td>
<td>15.3</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>4.8</td>
</tr>
<tr>
<td>Unknown</td>
<td>24</td>
<td>19.4</td>
</tr>
<tr>
<td>Total</td>
<td>124</td>
<td>99.9</td>
</tr>
</tbody>
</table>

Fig. 2. Kaplan–Meier curves for the baseline measurements of %fat, TSF, MAC and MAMC.
other hand, the main function of albumin is to provide osmotic pressure, which depends on hepatic function, and it is an acute-phase reactant. Therefore, we have explored the anthropometric parameters %fat, TSF, MAC and MAMC to determine if they could replace albumin and BMI in the routine care of haemodialysis patients. We found that %fat, TSF, MAC and MAMC were independent predictive parameters in all-cause patient mortality and potential predictors in different cause specific mortality. Although albumin was frequently found as an independent parameter of patient mortality, the question arose about its nutritional specificity.

The predictive values of all measured anthropometric parameters for patient mortality were similar, except for BMI. Moreover, all anthropometric parameters including BMI were closely correlated in spite of some differences among them. Both %fat and TSF measure body fat, MAC measures muscle mass and MAC both body fat and muscle mass. It is not surprising that MAC was the most predictive parameter in patients in whom protein-calorie malnutrition is common. On the other hand, BMI reflects both body fat and muscle mass and depends on other factors, like frame size and hydration status, more than the other anthropometric parameters examined in this study. That could be one reason why this factor was not predictive here, although it was found to be a risk factor in some other studies [4].

Our results suggested that muscle mass was more important for patient survival than body fat. Those individuals with higher muscle mass had a survival advantage that was underscored by the Kaplan–Meier curve for mid-arm muscle circumference. Smaller muscle mass could result from low caloric or low protein intake. It is well known that most apparently healthy haemodialysis patients suffer from both caloric and protein malnutrition, i.e. inadequate intake of both protein and calories [15]. As a consequence, protein stores including muscle mass must be utilized in the absence of sufficient calories. In addition, when fat stores are low or absent, the body’s only recourse for caloric sources is muscle, and it is catabolized. Although the conversion of protein to calories is a very inefficient process in which 25% of the protein is wasted, in the absence of sufficient caloric intake, the body has little recourse but to utilize protein especially when fat stores are exhausted. The high protein catabolic rate found in the present study confirmed that there was increased catabolism of protein in our patients (1.14 for men and 1.20 for women in the setting of a Kt/V of 1.16 instead of 1.0 g/kg/day as can be seen in stable dialysis patients). Our study suggested that small muscle mass, which could result from a low caloric or protein intake, was a more important risk factor for patient mortality than body fat.

Anthropometric parameters are not only good predictors of patient mortality, but also very simple and inexpensive to measure compared to long-established methods. Determination of %fat requires a skinfold caliper and uses a formula for calculation, but it could be compared with dual-

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hazard ratio (CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>1.84 (1.13–3.00)</td>
<td>0.01</td>
</tr>
<tr>
<td>Diabetes*</td>
<td>2.80 (1.49–5.26)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Chronic glomerulonephritis</td>
<td>0.48 (0.26–0.89)</td>
<td>0.02</td>
</tr>
<tr>
<td>Age (years)*</td>
<td>1.04 (1.02–1.06)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>1.74 (1.20–2.52)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Congestive heart failure*</td>
<td>2.22 (1.54–3.19)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Kt/V</td>
<td>0.08 (0.03–0.22)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>WBC binary</td>
<td>3.95 (2.14–7.26)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>0.98 (0.97–0.99)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.99 (0.99–0.99)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.90 (0.87–0.93)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>NPCR</td>
<td>0.06 (0.02–0.15)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Triceps skinfold</td>
<td>0.97 (0.94–0.99)</td>
<td>0.03</td>
</tr>
<tr>
<td>Mid-arm circumference</td>
<td>0.95 (0.92–0.98)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mid-arm muscle circumference</td>
<td>0.91 (0.87–0.96)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Hazard ratio, Exp (B); CI, 95% confidence interval of Exp (B); P, significance of coefficient.

*Time-unvarying covariate.

**Time-dependent covariates.**
Anthropometric parameters and patient survival

Energy X-ray absorptiometry (DEXA, 6). Although it is the best anthropometric method, MAC is simpler and only requires measurement of the circumference. At the same time, protein and calorie status of the patients is recorded, which gives an accurate prediction of survival. This was confirmed here, but MAMC is another simple and useful parameter for estimating protein status, although not overall protein status. To test if MAC is helpful only in cases of severe malnutrition, survival analysis of a subgroup without the MAC first quintile (determined separately for men and women) was done, and MAC remained an independent predictor of all-cause mortality (data not presented).

For more frequent use of these parameters, an important problem to be solved is poorly defined normal values. The normal value is usually taken at the 50th percentile value of a normal population without definition of the normal interval, which is more practical. Some authors, such as Harvey et al., used 5th to 15th percentile values as moderate depletion and less than fifth percentile values as severe depletion [15], while we considered interval values between the 5th and 95th percentiles as normal. The question arises whether such intervals for TSF, MAC and MAMC values in haemodialysis patients could be considered as normal as was a priori defined in our study. The %fat values found in our patients indicated that they were rather overweight, but those with values of TSF, MAC and MAMC lower than the fifth percentile most frequently had normal values for %fat. How to explain this difference?

In the absence of reference methods such as dual-energy X-ray absorptiometry (DEXA), we used %fat derived from anthropometric measures as the reference method for calorie intake because it is comparable with DEXA [6]. The observed disagreement between %fat and the other three anthropometric parameters could be the consequence of different distribution of body fat and physical inactivity.

In haemodialysis patients, body fat is distributed as in corticosteroid-treated patients, i.e. the amount of fat in the limbs is smaller than in the trunk [16]. Smaller muscle mass of the upper limbs could result from physical inactivity rather than a low calorie or protein intake. Our graphical analysis showed that 5th or 15th percentile values were far from real low normal values, as defined by Harvey et al. [17]. The graphical analysis used here enabled comparison of completely different parameters, which could not be done with other methods, i.e. the Bland–Altman test [18]. Better agreement was achieved when the lower level for TSF was set at 5.0 mm for men and 6.8 mm for women (instead of 4.5 and 11 mm, respectively) while the lower level for MAC was altered to 22.5 cm and 20.5 cm (instead of 26.4 cm and 23.2 cm) for men and women, respectively. These values were similar to the fifth percentile values of our patients (Table 4).

Another problem was comparison of MAMC with a reference method. Percentage of body fat measures calorie intake and not overall muscle mass. Malnutrition in haemodialysis patients is actually a protein-energy combination, but that does not mean that every patient with an energy deficit has a protein deficit of the same amount at the same time. Therefore, we attempted to compare MAMC with creatinine level, but poor agreement was found due to increased catabolism of protein and possibly because creatinine concentration depends not only on muscle mass but also on the balance between production and elimination. Nevertheless, 5th and 95th values in our patients are shown in Table 4. Normal values for TSF, MAC and MAMC remain to be further explored and defined in a larger population of haemodialysis patients.

It should not be overlooked that inter-operator error is common for anthropometric measurements. However, this error is smaller for MAC. In this study, all measurements were made by one investigator so that problem did not exist.

Unfortunately, our patients were not well dialysed, and this is an important drawback of the study. Target Kt/V was larger than 1.2, but due to the economic situation more than a half of the patients had Kt/V lower than 1.2 [19]. Therefore, skinfold thickness could overestimate the patient’s nutritional status, as was found in children [20]. Fluid overload could increase weight, alter regional distribution of both fat and lean mass and lead to either overestimation or underestimation of nutritional status. These changes may impact correlation between %fat and the other parameters outlined in Figure 1. It may also be a reason for the discrepancies in weights noted among both the men and the women. However, inadequately dialysed patients also suffer from protein and caloric malnutrition, and nutritional parameters were negative predictors of mortality. Testing correlation in a subdialysed group revealed similar or even higher values for anthropometric parameters compared with all patients, and the number of possibly overload patients in the group of subdialysed patients was small. When the first Kt/V tertile was removed from analysis, MAC remained independent and the most important predictor among the anthropometric variables. The same relation existed when only the third Kt/V tertile was analysed (data not presented).

Traditional anthropometric parameters (%fat derived from skinfolds as well as triceps skinfold, mid-arm circumference and mid-arm muscle circumference) were found to be independent predictors of all-cause mortality in this study, and MAC was the most predictive one.

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Conflict of interest statement. None of the authors has any conflict of interest.

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Screening for encapsulating peritoneal sclerosis in patients on peritoneal dialysis: role of CT scanning

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Abstract

Background. We previously validated a scoring system for abdominal/pelvic CT scans in patients with symptomatic encapsulating peritoneal sclerosis (EPS). CT scans of patients with symptomatic EPS were significantly different from control peritoneal dialysis (PD) or haemodialysis patient scans; scans performed before EPS was clinically evident were near normal in 9 of 13 patients. We have now investigated CT scanning as a screening modality in a larger group of patients on long-term PD.

Methods. Pre-diagnostic CT scans performed in 20 patients for routine screening or other indications at least 3 months before EPS developed, and later diagnostic scans when EPS was clinically evident, were scored by three radiologists. The control group included CT scans of 20 PD patients who had not developed EPS (median follow-up 2.25 years). Analysis was by non-parametric tests. CT scores ranged from 0 to 22; >2.5 was considered abnormal.

Results. Clinical EPS only developed after transplantation or transfer to HD. Diagnostic scans scored significantly higher than pre-diagnostic or control scans (median scores 9, 2 and 1; P < 0.001), confirming previous work. The pre-EPS diagnosis of 12 asymptomatic patients had a median CT score = 1.75, similar to the control group. Eight patients