Nephrol Dial Transplant (2009) 24: 225–230
doi: 10.1093/ndt/gfn449
Advance Access publication 8 August 2008

Original Article

NDT
Nephrology Dialysis Transplantation

Symptom clusters in incident dialysis patients: associations with clinical variables and quality of life

Melissa S. Y. Thong[1], Sandra van Dijk[2], Marlies Noordzij[3], Elisabeth W. Boeschoten[4], Raymond T. Krediet[5], Friedo W. Dekker[1] and Adrian A. Kaptein[2] for the NECOSAD Study Group*

[1]Department of Clinical Epidemiology, [2]Department of Medical Psychology, Leiden University Medical Centre, Leiden, [3]Department of Clinical Epidemiology, Biostatistics, and Bioinformatics, Academic Medical Center, University of Amsterdam, [4]Hans Mak Institute, Naarden and [5]Department of Nephrology, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands

Abstract

Background. To date, the pathophysiology underlying symptoms in renal patients is still unclear. Symptom management research suggests that identification of related clusters of symptoms could provide insight into underlying determinants associated with multiple symptom experience. Theoretically, symptoms within a cluster could have a synergistic relationship. We aimed to identify symptom clusters in incident dialysis patients, and investigated associations between symptom clusters, clinical variables, functional status as measured by the Karnofsky Index and quality of life.

Methods. 1553 haemodialysis (HD) and peritoneal dialysis (PD) patients completed the Kidney Disease Quality of Life Short Form symptom/problem list at 3 months after the start of dialysis. Principal component analysis using varimax rotation was used to identify symptom clusters.

Results. Patients were bothered by an average of 2.8 ($\pm$2.4) symptoms of 'moderate bother' or more. Three clusters were identified, explaining 49% of the total variance. All clusters showed strong negative associations with the SF-36 quality of life dimensions (-0.142 to -0.593) and with functional status (-0.130 to -0.332) in HD and PD patients. In contrast, only the clinical variables serum albumin (-0.084 to -0.232) and haemoglobin (-0.068 to -0.126) were associated with all clusters in HD patients, and Kt/V_{urea} (-0.089 to -0.125) in PD patients.

Conclusions. Symptom clustering does not explain the lack of meaningful associations between symptoms and clinical variables. Strong associations of symptom clusters with quality of life dimensions suggest that psychological factors could better explain symptom burden. Patients' perceptions of symptoms should be routinely assessed as part of clinical care to improve self-management strategies.

Keywords: dialysis; ESRD; health-related quality of life; symptoms; symptom clusters

Introduction

Patients undergoing dialysis treatment experience a plethora of disease- and treatment-related symptoms. High symptom burden is associated with reduced health-related quality of life (HRQOL) [1], and increased morbidity and mortality in dialysis patients [2]. Symptoms can be hard to treat, and the pathophysiology underlying these symptoms is still unclear [3]. Weak associations are often found between symptoms and clinical variables [3,4].

Symptom clustering is a relatively new topic currently explored in symptom management research. Symptom clusters refer to concurrent symptoms related to each other [5]. These concurrent symptoms, in theory, can have a synergistic relationship. Clinical relevance of symptom cluster research could provide insights into common underlying mechanism(s) associated with multiple symptoms.

Research on symptom clustering in dialysis patients is scarce. To our knowledge, only two studies have identified symptom clusters in dialysis patients [6,7]. Both these studies had small samples limited to haemodialysis (HD) patients and did not investigate the correlations of the symptom clusters with clinical variables.

Our objectives are to identify symptom clusters in incident HD and peritoneal dialysis (PD) patients and examine associations between symptom clusters, clinical variables

Correspondence and offprint requests to: Melissa Thong, Department of Clinical Epidemiology, Leiden University Medical Centre, PO Box 9600, 2300 RC Leiden, The Netherlands. Tel: +31-71-526-4394; Fax: +31-71-526-6994; E-mail: S.Y.M.Thong@lumc.nl

*A.J. Apperloo, J.A. Bijlsma, M. Boekhout, W.H. Boer, P.J.M. van der Boog, H.R. Büller, M. van Buren, F.Th. de Charro, C.J. Doorenbos, M.A. van den Dorpel, A. van Es, W.J. Fagel, G.W. Feith, C.W.H. de Fijter, L.A.M. Frenken, J.A.C.A. van Geelen, P.G.G. Gerlag, W. Grave, J.P.M.C. Gorgels, R.M. Huisman, K.J. Jager, K. Jie, W.A.H. Koning-Mulder, M.I. Koolen, T.K. Kremer Hovinga, A.T.J. Lavrijssen, A.J. Luik, J. van der Meulen, K. J. Parlevliet, M.H.M. Raasveld, F.M. van der Sande, M.J.M. Schonck, M.M.J. Schuurmans, C.E.H. Siegert, C.A. Stegeman, P. Stevens, J.G.P. Thijssen, R.M. Valentijn, G.H. Vastenburg, C.A. Verburgh, H.H. Vincent, P.F. Vos.

and HRQOL. Clinical implications of our study include identifying symptom clusters in dialysis patients that could provide a theoretical framework to study the possible determinants underlying symptom experience, and thereby assist in symptom management.

Methods

Patient sample

Between January 1997 and January 2007, incident dialysis patients from 38 dialysis centres throughout the Netherlands were recruited with informed consent to participate in The Netherlands Co-operative Study on the Adequacy of Dialysis (NECOSAD-2) [8], a prospective observational study investigating the adequacy of care for patients on dialysis treatment. Eligibility included being over 18 years of age, with no previous history of renal replacement therapy, being alive at 3 months (baseline) and having a symptom score assessed at baseline. A baseline of 3 months was chosen to allow for patients' treatment modality and clinical condition to be stabilized. The study was approved by all local medical ethics committees.

Data collection

Baseline information on demographics, clinical parameters and physical symptoms was collected at 3 months after the start of dialysis. Demographic data collected were gender, age, marital status and educational level. Clinical information obtained included comorbidity, primary cause of kidney disease, residual renal function, erythropoietin use, serum albumin, C-reactive protein (CRP), plasma calcium (corrected for serum albumin), plasma phosphorus, intact parathyroid hormone (iPTH), body mass index (BMI), nutritional status, smoking and functional status. Comorbidity was determined by the 3-point Davies score [9], which was calculated according to the type and number of comorbidities present, whilst the primary cause of kidney disease was classified using the European Renal Association–European Dialysis and Transplantation Association codes. Residual renal function parameters included the residual glomerular filtration rate (rGFR), calculated as the mean renal clearance of urine and creatinine corrected for body surface. Dialysis dose was expressed as Kt/V_{urea} per week, which was calculated as renal urea clearance corrected for the urea distribution volume according to Watson *et al.* [10]. A second-generation Daugirdas formula was used to calculate dialysis urea clearance in HD patients, while Kt/V_{urea} in PD patients was derived from a 24-h dialysate collection [11]. Dietary protein intake was assessed as protein catabolic rate (PCR) [12] for HD patients, and as protein nitrogen appearance (PNA) [13] for PD patients. Both values (nPCR and nPNA) were normalized to actual body weight. Nutritional status of patients was assessed by the dialysis staff using the standardized 7-point Subjective Global Assessment (SGA) scale [14]. The dialysis staff assessed patients' functional status using the Karnofsky Index [15].

Patients' symptomatology was assessed using the symptom/problem list in the disease-specific Kidney Disease Quality of Life Short Form (KDQOL-SF^{TM}). The KDQOL-SF^{TM} is a reliable and validated health measure, consisting of items assessing quality of life specific to individuals on dialysis treatment [16]. Patients were given the KDQOL-SF^{TM} questionnaire during their clinical visits with instructions to return the filled questionnaire via pre-paid post within a week.

Twelve symptoms from the symptoms/problem list of the KDQOL-SF^{TM} were assessed: muscle soreness, chest pains, cramps, itch, dry skin, shortness of breath, feeling dizzy/faint, lack of appetite, feeling 'squeezed out', numbness in the extremities, nausea and problems with access site (HD) or shunt (PD). Patients were asked to rate how bothered they were by each symptom over the past 4 weeks on a 5-point scale (1 = no bother at all; 2 = somewhat; 3 = moderately; 4 = very much and 5 = extremely bothered). In this study, the prevalence of a symptom was defined as having a score of 2 or higher on that symptom.

Quality of life was assessed with the SF-36, a generic HRQOL instrument measuring eight dimensions: physical functioning, role limitations due to physical problems, role limitations due to emotional problems, social functioning, mental health, vitality, body pain and general health perception. Items in each subscale are added together to form subscale scores, which are transformed to a 0–100 scale, with higher scores indicating a better HRQOL. The eight subscale scores were further combined into the physical (PCS) and mental (MCS) component summary scores. The SF-36 is a reliable and valid instrument used extensively in different population and patient samples, including dialysis patients [17].

Statistical analyses

Differences between continuous variables were assessed using the Mann–Whitney test, whilst categorical outcomes were tested using the chi-square test. Twelve symptoms from the KDQOL were entered into a principal component analysis (PCA) using varimax rotation. PCA is a suitable technique to identify underlying dimensions as it reduces multiple variables into smaller number of variables or components that describe the data most efficiently [18]. Varimax rotation was used as it maximizes the variance of the loadings within each component whilst assuming the independence of the component structure [18]. Components with Eigenvalues >1 were retained for further analysis. The Eigenvalue is equivalent to the amount of variance explained by a component. Items in each resultant component were summed to form the subscale score. Reliability (Cronbach's alpha) for the items within each component was also examined. To assess the association of comorbidity with the symptom clusters, comorbid conditions of angina pectoris, myocardial infarct, cardiac failure, coronary artery disease, cardiovascular accident and peripheral vascular disease were combined to indicate the presence of cardiovascular diseases (CVD). Significance levels were determined at $P \leq 0.05$. SPSS version 12.0 was used for the statistical analyses.

Results

Of the 1712 eligible patients alive at 3 months after start of dialysis, 159 (9.3%) patients had a missing baseline symptom score. Patients with a missing symptom score had higher levels of CRP, poorer nutritional status and lower functional ability compared with those with a symptom score.

Table 1 outlines the baseline characteristics of HD and PD patients. More males were treated with PD. Compared with HD patients, PD patients were younger, were more likely to be married and had a higher level of education. In terms of clinical parameters, PD patients more often had glomerulonephritis as the primary cause of kidney disease, had a higher rGFR, had a higher level of haemoglobin, had a higher level of calcium, were better nourished, had less comorbid illnesses, had lower prevalence of erythropoietin use, had lower CRP and had a lower phosphorus level. Furthermore, PD patients scored higher on all SF-36 quality of life dimensions, and had higher level of functioning when compared with HD patients.

Table 1. Patients' demographics, clinical characteristics, physical functioning and quality of life (SF-36) scores at baseline

	HD ($N = 1010$)	PD ($N = 543$)
Male*	573 (56.7%)	347 (63.9%)
Age*	63.2 ± 13.8	53.3 ± 14.6
Marital status*		
Married	656 (65.0%)	399 (73.5%)
Education[a]*		
Low	578 (57.2%)	245 (45.1%)
Primary cause of renal failure*		
Diabetes mellitus	142 (14.1%)	82 (15.1%)
Glomerulonephritis	98 (9.7%)	110 (20.3%)
Renal vascular disease	204 (20.2%)	62 (11.4%)
Davies comorbidity score*		
None	416 (41.2%)	315 (58.0%)
Medium	477 (47.2%)	183 (33.7%)
High	100 (9.9%)	37 (6.8%)
rGFR (mL/min/1.73 m^2)*	3.9 ± 2.9	4.6 ± 3.3
Kt/V_{urea}/week	3.4 ± 0.9	2.3 ± 0.6
Haemoglobin (g/dL)*	10.7 ± 1.4	12.0 ± 1.5
Use of erythropoietin*		
Yes	899 (89.0%)	381 (70.2%)
Serum albumin (g/dL)	3.6 ± 0.5	3.6 ± 0.5
CRP (mg/L)*	13.5 ± 25.8	9.9 ± 19.9
Calcium (mg/dL)[b]*	9.6 ± 1.0	10.0 ± 1.0
Phosphorus (mg/dL)*	5.8 ± 1.8	5.3 ± 1.4
iPTH (pg/mL)	224.6 ± 306.0	205.1 ± 236.9
BMI (kg/m^2)	24.7 ± 4.3	24.6 ± 3.7
SGA score[c]*		
5 or less	278 (27.5%)	87 (16.1%)
6–7	615 (60.9%)	411 (75.7%)
nPCR/nPNA (g/kg/day)	1.0 ± 0.2	1.0 ± 0.3
Smoking		
Non-smoking	687 (68.0%)	364 (67.1%)
Karnofsky Index*	78.0 ± 14.8	84.9 ± 12.2
SF-36, physical functioning*	48.3 ± 28.4	61.2 ± 25.4
SF-36, role functioning (physical)*	25.9 ± 36.5	35.7 ± 40.0
SF-36, role functioning (emotional)*	49.8 ± 44.0	63.3 ± 41.9
SF-36, social functioning*	62.4 ± 27.7	68.3 ± 36.6
SF-36, bodily pain*	63.5 ± 28.4	72.8 ± 24.8
SF-36, mental functioning*	67.6 ± 20.0	71.1 ± 19.3
SF-36, vitality*	48.7 ± 21.2	52.0 ± 20.6
SF-36, general health*	41.6 ± 18.9	46.7 ± 20.3
SF-36 PCS*	38.8 ± 9.7	42.9 ± 9.0
SF-36 MCS*	43.7 ± 11.3	45.3 ± 11.0

Values presented are means (± SD) unless otherwise stated.
*$P < .05$, HD versus PD.
[a]Education: low (primary school, lower vocational training; high (lower general secondary education, pre-university education, high vocational training, university).
[b]Calcium value corrected for serum albumin.
[c]SGA: subjective global assessment. Higher scores indicate better nutritional status (6–7 = well nourished, ≤5 = malnourished).

The most prevalent symptoms include sore muscles, itch, dry skin and cramps (as reported by patients of being 'some bother' or more), while patients had least complaints of problems with access site/shunt and chest pains (Figure 1). No association was found between symptoms and seasonal variation. Our sample experienced on average 2.8 (± 2.4) concurrent symptoms that they reported of being at least of 'moderate bother' (a score of 3 or higher on the symptom scale). Nearly 49% of the sample reported of being bothered with three or more symptoms that were of moderate bother or higher.

Exploratory principal component analysis extracted three clusters with Eigenvalues >1 from 11 symptoms (Table 2). The symptom of problem with access site/shunt did not load significantly onto any of the three symptom clusters. Total amount of variance explained by these three statistically derived clusters was 49%. Cronbach's alpha for the clusters ranged from 0.58 to 0.70.

Cluster 1 included symptoms such as shortness of breath, feeling faint/dizzy, poor appetite, feeling 'squeezed out' and feeling nauseous. As these symptoms are often indicative of uraemia, we labelled this cluster as 'general symptoms of the uraemic syndrome'. The second cluster consisted of symptoms such as sore muscles, chest pain and numbness in the hands/feet. These symptoms could reflect disturbances in patients' neuromuscular functions, and were therefore labelled 'neuromuscular problems'. The symptoms of itch and dry skin made up cluster 3, which could reflect an underlying dimension of 'skin problems'.

A three-cluster solution for HD and PD patients separately gave no materially different results, and had similar cluster loadings as reported in Table 2.

Table 3 outlines the correlations of the three clusters with HRQOL, demographic and clinical variables, separate for HD and PD patients. In both groups, all three clusters were significantly correlated with each other (0.350–0.502) and negatively correlated with each of the SF-36 subscales, ranging from −0.142 to −0.593. Similarly, the Karnofsky Index scores were negatively correlated with all three clusters in both the HD and PD samples. On the other hand, correlations with clinical parameters were less strong. Among HD patients, only serum albumin and haemoglobin were significantly correlated with all three symptom clusters. CVD was correlated with cluster 1, while diabetes mellitus was negatively correlated with both cluster 1 and cluster 2 in the HD sample. In the PD group, Kt/V_{urea} was significantly correlated with all three symptom clusters, whilst cluster 3 was significantly correlated with rGFR, phosphorus and calcium. Both CVD and diabetes mellitus were significantly correlated with cluster 2 only in the PD sample.

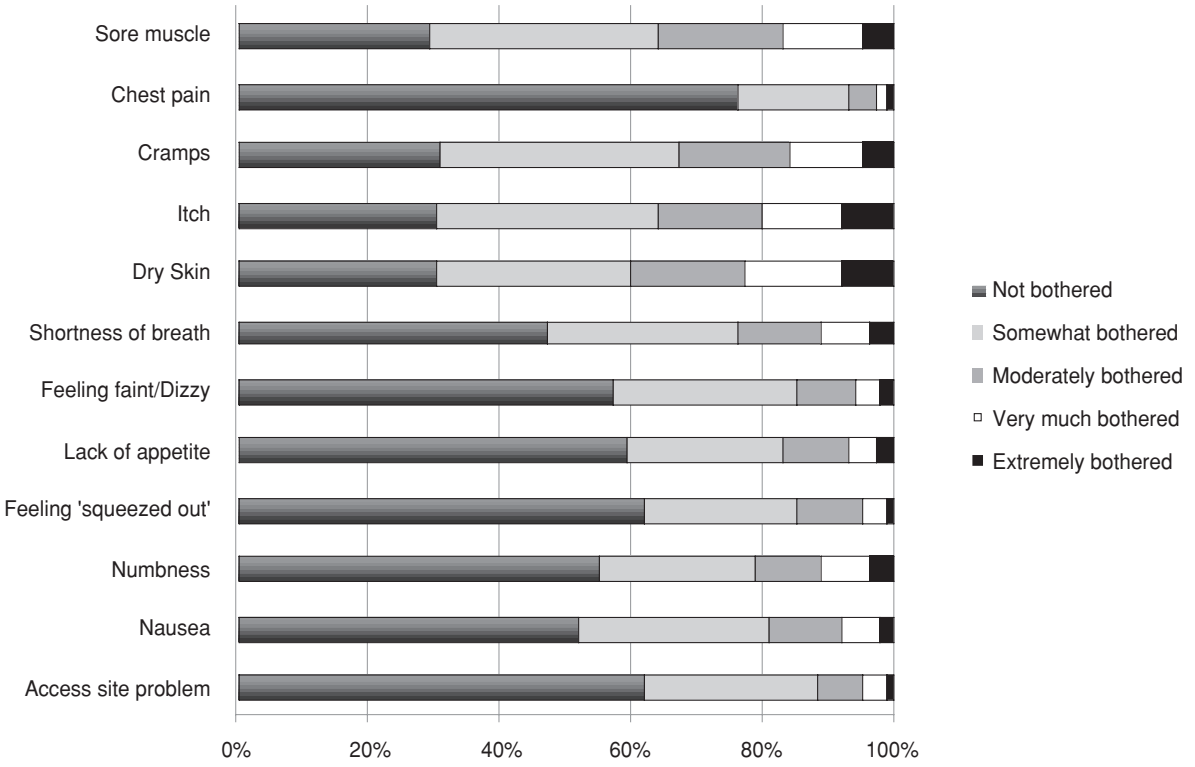

Fig. 1. Prevalence of symptom distress of whole sample.

Table 2. Symptom loadings of three-cluster solution

Symptom	Cluster 1	Cluster 2	Cluster 3
Short breath	**0.51**	0.44	−0.08
Dizzy/faint	**0.57**	0.37	0.06
Lack of appetite	**0.79**	−0.15	0.17
Feeling 'squeezed out'	**0.53**	0.28	0.20
Nausea	**0.69**	0.13	0.21
Sore muscle	0.07	**0.70**	0.25
Chest pain	0.40	**0.54**	−0.30
Cramps	0.05	**0.60**	0.24
Numbness in extremities	0.16	**0.56**	0.12
Itch	0.18	0.22	**0.76**
Dry skin	0.20	0.23	**0.76**
Variance (%)	30.1	9.8	9.1
Cronbach's alpha	0.70	0.58	0.68

Values in bold indicate the factor loading of the symptom in each symptom cluster.

Discussion

Our study showed that the burden of multiple symptoms experienced by incident HD and PD patients is extensive. Principal component analysis of the symptoms yielded three clusters in our sample. The symptom clusters were strongly associated with HRQOL dimensions and physical functioning. Clustering of symptoms did not improve its association with clinical parameters in dialysis patients as all symptom clusters in our study showed weak or absent association with a range of clinical variables.

The weak associations between symptoms and clinical variables are in line with other studies on dialysis patients [3,4]. We had hypothesized that symptom clustering might improve the weak association between symptoms and clinical variables compared with other methods of assessment used in previous studies. Previous methods of assessing individual symptoms [19] or the use of a total symptom score calculated from a symptom list [8] might not adequately measure the symptom experience, as dialysis patients often experience multiple symptoms that could reflect a multidimensional rather than unidimensional phenomenon as assumed with the use of overall scores. Although we identified symptom clusters with seemingly clinical relevance, nevertheless, symptom clustering showed similar weak associations with clinical variables, as in previous studies using other methods of assessment.

Clinically, it is difficult to understand that patient-reported 'uraemic symptoms' are hardly related to objective clinical indicators of uraemia. Although clinical variables such as rGFR, haemoglobin, serum albumin, CRP, calcium and phosphorus levels were associated in a statistically significant manner with some or all of the symptom clusters, these associations might be due to our large sample size and may not be of clinical significance.

With the poor associations between symptom clusters and clinical variables, we postulate that psychological factors are more important determinants of symptom burden. After all, symptoms are defined as the subjective perceptions of physical, emotional or cognitive changes as experienced by the patient [20]. Therefore, perceptions of symptom burden are more likely to be influenced by

Table 3. Correlations of the three symptom subscales with SF-36 subscales, demographics and clinical variables by therapy at baseline (3 months from start of dialysis)

	HD			PD		
	Cluster 1	Cluster 2	Cluster 3	Cluster 1	Cluster 2	Cluster 3
Cluster 2	**0.502****			**0.464****		
Cluster 3	**0.396****	**0.350****		**0.418****	**0.443****	
SF-36, physical functioning	**−0.414****	**−0.311****	**−0.272****	**−0.449****	**−0.411****	**−0.295****
SF-36, role functioning (physical)	**−0.387****	**−0.290****	**−0.255****	**−0.364****	**−0.297****	**−0.202****
SF-36, role functioning (emotional)	**−0.368****	**−0.243****	**−0.218****	**−0.296****	**−0.248****	**−0.142****
SF-36, social functioning	**−0.487****	**−0.300****	**−0.262****	**−0.434****	**−0.350****	**−0.265****
SF-36, body pain	**−0.465****	**−0.450****	**−0.286****	**−0.426****	**−0.463****	**−0.257****
SF-36, mental functioning	**−0.481****	**−0.292****	**−0.214****	**−0.446****	**−0.352****	**−0.300****
SF-36, vitality	**−0.593****	**−0.343****	**−0.327****	**−0.548****	**−0.364****	**−0.332****
SF-36, general health	**−0.496****	**−0.335****	**−0.270****	**−0.381****	**−0.324****	**−0.233****
SF-36, physical component score	**−0.473****	**−0.413****	**−0.329****	**−0.451****	**−0.433****	**−0.277****
SF-36, mental component score	**−0.492****	**−0.262****	**−0.216****	**−0.416****	**−0.296****	**−0.239****
Karnofsky Index	**−0.332****	**−0.130****	**−0.226****	**−0.321****	**−0.315****	**−0.220****
Age	−0.020	−0.038	0.034	0.050	**0.149****	0.052
BMI	0.003	**−0.109****	0.064	0.008	0.068	−0.026
RGFR	−0.037	0.008	−0.030	−0.073	−0.052	**−0.127****
Kt/V_{urea}/week	0.012	0.009	0.029	**−0.103***	**−0.125****	**−0.089***
CRP	**0.142****	0.029	0.068	0.096	0.034	0.049
Serum albumin	**−0.232****	**−0.084***	**−0.121***	−0.072	−0.015	−0.036
NPCR	**−0.108****	−0.011	−0.029			
NPNA				−0.002	−0.006	0.011
Calcium[a]	−0.031	−0.009	**0.074***	−0.019	−0.063	**0.089***
Phosphorus	−0.002	−0.057	0.023	−0.025	0.079	**0.143****
Haemoglobin	**−0.126****	**−0.068***	**−0.079***	−0.071	**−0.089***	−0.071
iPTH (pg/mL)	−0.033	0.020	−0.003	−0.034	−0.002	−0.011
Comorbidity (CVD)[b]	0.066	**0.114****	0.012	0.023	**0.217****	0.042
Comorbidity (diabetes mellitus)	**−0.079***	**−0.103****	−0.060	−0.056	**−0.143***	0.045

Cluster 1: shortness of breath, feeling dizzy/faint, lack of appetite, feeling 'squeezed out', nausea.
Cluster 2: sore muscles, chest pain, cramps, numbness in extremities.
Cluster 3: itch, dry skin.
Values in bold: $^{**}P < .001$; $^{*}P < .05$.
[a]Calcium value corrected for serum albumin.
[b]CVD = cardiovascular disease (includes angina pectoris, myocardial infarct, cardiac failure, coronary artery disease, cardiovascular accident, peripheral vascular disease).

psychological factors such as personality or cognitions [20]. Dialysis patients who perceive having more control and fewer consequences due to their disease had better health outcomes [21].

This implies that clinical interventions aimed at reducing uraemia and improving patients' quality of life might not necessarily correlate meaningfully with patients' subjective health assessments. While this should not deter clinicians from striving to optimize clinical treatment of uraemia as indicated by symptom reduction, symptoms are often determined in a small part by objective clinical indicators. Therefore, clinicians can augment their care provision by incorporating both objective and subjective indicators into patients' assessment and treatment protocol [22].

High symptom burden impacts negatively on patients' HRQOL. The chronic nature of dialysis means that the patients often have sole responsibility for the daily management of their disease. Identification of patients' symptom (mis)perceptions can assist patients in selecting appropriate strategies for the self-management of their symptom burden [23]. Self-management refers to the health promotion and patient education programmes developed to encourage behaviour change and assist in adjustment for a chronic illness [24]. A small experimental study designed to reshape the self-representation of HD patients' coping skills on disease adjustment reported that the self-representation condition was more effective in improving adjustment, and alleviating depression and physical symptoms compared to two other treatment conditions, problem disclosure and control [25].

Comparing the symptom clusters identified in our study with those reported in other studies is difficult as the symptoms and the number of symptoms assessed in the different studies are varied [6,26]. Nevertheless, some similarities in symptom loadings between our study and others were identified. For example, cluster 2 ('neuromuscular problems') in our study shared some similarity with the 'mobility index' of Curtin *et al*. [6], which comprised numbness in extremities, muscle soreness, muscle weakness and bone/joint pain. Chiou [26] reported a 'disturbance in muscular function' cluster comprising seven symptoms. Three of these symptoms (feeling dizzy/faint, shortness of breath and poor appetite) were similarly loaded onto cluster 1 ('general symptoms of uraemic syndrome') in our study. We interpreted these symptoms as reflecting an underlying uraemic syndrome rather than as disturbances in muscular function as suggested by Chiou [26].

The subjectivity in interpretation of symptom clusters is a possible limitation of our study. The clinical descriptions

we have provided are subjective and debatable. Although principal component analysis is useful in data reduction and identifying possible underlying dimensions, nevertheless the subjective inclusion and interpretation of variables within each cluster/component could mean that our cluster solution might not have provided an adequate explanation for the data.

Secondly, we assessed the severity of 12 symptoms with the symptom problem list of the KDQOL-SF. This list with its predetermined symptoms has no free fields for patients to describe other possible symptoms. As such, our assessment might not encompass the whole symptom experience of dialysis patients.

Data on patients' illness perceptions, affect status and strategies for self-management were not collected in our study. Future research could explore in greater detail the symptomatology experienced by dialysis patients by gathering information on, for instance, illness perceptions, self-efficacy and self-management strategies. Such information can be incorporated into psycho-educational programmes to promote cognitive change so as to improve patients' self-efficacy and, thereby, self-management skills [23].

In conclusion, our study shows that dialysis patients experience concurrent symptoms, from which distinct clusters could be derived. These symptom clusters are all negatively associated with HRQOL dimensions, but have weak correlations with clinical variables. To reduce patients' symptom burden, patients' cognitions and beliefs should be routinely assessed to ensure that their self-management strategies can be appropriately supported.

Acknowledgements. This work was supported in part by unrestricted grants from Baxter Healthcare and the Dutch Kidney Foundation. The funding sources were neither involved in the collection, interpretation and analysis of the data nor in the decision for the writing and submission of this report for publication. We thank the nursing staff of the participating dialysis centres and the staff of the NECOSAD trial office for their invaluable assistance in the collection and management of data for this study.

Conflict of interest statement. None declared.

References

1. Murtagh FE, Addington-Hall J, Higginson IJ. The prevalence of symptoms in end-stage renal disease: a systematic review. *Adv Chronic Kidney Dis* 2007; 14: 82–99
2. Mapes DL, Lopes AA, Satayathum S *et al*. Health-related quality of life as a predictor of mortality and hospitalization: The Dialysis Outcomes and Practice Patterns Study (DOPPS). *Kidney Int* 2003; 64: 339–349
3. Barrett BJ, Vavasour HM, Major A *et al*. Clinical and psychological correlates of somatic symptoms in patients on dialysis. *Nephron* 1990; 55: 10–15
4. Bakewell AB, Higgins RM, Edmunds ME. Quality of life in peritoneal dialysis patients: decline over time and association with clinical outcomes. *Kidney Int* 2002; 61: 239–248
5. Miaskowski C, Aouizerat BE, Dodd M *et al*. Conceptual issues in symptom clusters research and their implications for quality-of-life assessment in patients with cancer. *J Natl Cancer Inst Monogr* 2007; 37: 39–46
6. Curtin RB, Bultman DC, Thomas-Hawkins C *et al*. Hemodialysis patients' symptom experiences: effects on physical and mental functioning. *Nephrol Nurs J* 2002; 29: 562,567–574
7. Jablonski A. The multidimensional characteristics of symptoms reported by patients on hemodialysis. *Nephrol Nurs J* 2007; 34: 29–37
8. Merkus MP, Jager KJ, Dekker FW *et al*. Physical symptoms and quality of life in patients on chronic dialysis: Results of The Netherlands Cooperative Study on Adequacy of Dialysis (NECOSAD). *Nephrol Dial Transplant* 1999; 14: 1163–1170
9. Davies SJ, Russell L, Bryan J *et al*. Comorbidity, urea kinetics, and appetite in continuous ambulatory peritoneal dialysis patients: their interrelationship and prediction of survival. *Am J Kidney Dis* 1995; 26: 353–361
10. Watson PE, Watson ID, Batt RD. Total body water volumes for adult males and females estimated from simple anthropometric measurements. *Am J Clin Nutr* 1980; 33: 27–39
11. Daugirdas JT. Second generation logarithmic estimates of single pool variable volume Kt/V: an analysis of error. *J Am Soc Nephrol* 1993; 4: 1205–1213
12. Daugirdas JT. The post:pre-dialysis plasma urea nitrogen ratio to estimate Kt/V and NPCR: mathematical modeling. *Int J Artif Organs* 1989; 12: 411–419
13. Bergstrom J, Furst P, Alvestrand A *et al*. Protein and energy intake, nitrogen balance and nitrogen losses in patients treated with continuous ambulatory peritoneal dialysis. *Kidney Int* 1993; 44: 1048–1057
14. Visser R, Dekker FW, Boeschoten EW *et al*. Reliability of the 7-point subjective global assessment scale in assessing nutritional status of dialysis patients. *Adv Perit Dial* 1999; 15: 222–225
15. Karnofsky DA, Burcherval JH. The clinical evaluation of chemotherapeutic agents in cancer. In: Macleod CM (ed.). *Evaluation of chemotherapeutic agents in cancer*. New York: Columbia University Press, 1949, 191–205
16. Korevaar JC, Merkus MP, Jansen MA *et al*. Validation of the KDQOL-SF: a dialysis-targeted health measure. *Qual Life Res* 2002; 11: 437–447
17. Mingardi G, Cornalba L, Cortinovis E *et al*. Health-related quality of life in dialysis patients: a report from an Italian study using the SF-36 Health Survey. DIA-QOL Group. *Nephrol Dial Transplant* 1999; 14: 1503–1510
18. Tabachnick BG, Fidell LS. *Using Multivariate Statistics*, 5th edn. Boston: Pearson/Allyn & Bacon 2007
19. Davison SN. Pain in hemodialysis patients: prevalence, cause, severity, and management. *Am J Kidney Dis* 2003; 42: 1239–1247
20. Pennebaker JW. *The Psychology of Physical Symptoms*. New York: Springer, 1982
21. Timmers L, Thong M, Dekker FW *et al*. Illness perceptions in dialysis patients and their association with quality of life. *Psychol Health* 2008; 23: 679–690
22. Cukor D, Cohen SD, Peterson RA *et al*. Psychosocial aspects of chronic illness: ESRD as a paradigmatic illness. *J Am Soc Nephrol* 2007; 18: 3042–3055
23. Petrie KJ, Cameron LD, Ellis CJ *et al*. Changing illness perceptions after myocardial infarction: an early intervention randomized controlled trial. *Psychosom Med* 2002; 64: 580–586
24. Lorig KR, Holman HR. Self-management education: history, definition, outcomes, and mechanisms. *Ann Behav Med* 2003; 26: 1–7
25. Leake R, Friend R, Wadhwa N. Improving adjustment to chronic illness through strategic self-representation: an experimental study on a renal dialysis unit. *Health Psychol* 1999; 18: 54–62
26. Chiou CP. Development and psychometric assessment of the physical symptom distress scale. *J Pain Symptom Manage* 1998; 16: 87–95

Received for publication: 19.10.07
Accepted in revised form: 14.7.08