Symptom Burden Clustering in Chronic Kidney Disease Stage 5

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Abstract

Patients with Chronic Kidney Disease (CKD) stage 5, experience multiple symptoms that negatively affect the health-related quality of life (HRQoL). This study examined the cluster of symptoms and their association with disease severity and comorbidities. The study sample included 123 patients with CKD stage 5; 60 patients were in the dialysis group and 63 patients in the Conservative Kidney Management group. Symptom data were collected using the Spanish modified version of POS-S Renal, a validated questionnaire to assess symptoms in this population. Over half of the patients described weakness, difficulty sleeping, and feeling depressed. Two symptom clusters were identified. There was no significant statistical correlation between disease severity and symptoms and between comorbidities and symptoms. The tendency of these symptoms to occur together has implications for improving symptom management in this population. Routine symptom assessment can be useful in clinical and research settings.

Keywords: advanced chronic kidney disease, nursing, symptom evaluation, symptom cluster

Introduction

Chronic kidney disease (CKD) is a public health problem with a high incidence and prevalence that is expected to rise over the next years(Otero, de Francisco, Gayoso, García, & EPIRCE Study Group, 2010).In Spain, the prevalence of Advanced Chronic Kidney Disease (ACKD) (defined as CKD at stage 4 or 5 with a glomerular filtration rate < 30ml/min/1.73m^2) exceeds 1,000 patients per million population(pmp)(National Kidney Foundation, 2002;Otero et al., 2010; Stevens, Levin, & Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Development Work Group Members, 2013). The number of patients receiving renal replacement therapy (RRT) has steadily increased in developed countries. Currently, almost all patients with ACKD enter a RRT program. According to the European Association of Nephrology, the average rate of patients who continued treatment with dialysis was 637 per million inhabitants in 2010 (Otero et al., 2010).

Patients with ACKD have a wide range of physical and psychological symptoms and high costs of care (Davison et al., 2015). From the initial stages of ACKD, the accompanying symptoms are often highly variable and negatively affect the health-related quality of life (HRQoL)(Abdel-Kader, Unruh, &Weisbord, 2009; Iyasere & Brown, 2014).Among the most prevalent symptoms of these patients are weakness, pruritus, constipation, pain, changes in sleep patterns, anxiety, dyspnoea, nausea, restless legs, and depression(Murtagh, Addington-Hall, & Higginson, 2007;O'Connor& Kumar, 2012).In addition, emotional symptoms such as anxiety and depression are related to higher levels of somatic symptoms(Perales-Montilla, Duschek, & Reyes-Del Paso, 2013). In this respect, patients with ACKD commonly experience multiple symptoms and nurses play an essential role in their symptom assessment and management. Most of these studies have focused on the evaluation of single or multiple

symptoms (Murtagh, Addington-Hall, & Higginson, 2007; O'Connor & Kumar, 2012). However, symptoms can occur together and can be related to each other as part of a cluster. Symptom cluster research can increase our understanding of symptomatology, improving symptom management in this population. In this regard, symptom cluster research is an area of special interest in ACKD (Almutary, Douglas, & Bonner, 2016; Jablonsky, 2007).

As the uncontrolled symptoms in this population contribute to greater suffering, the symptoms management in earlier phases of the disease is a priority (Mannset al., 2014; O'Hare, Armistead, Schrag, Diamond, & Moss, 2014; Steinhauser et al., 2000). Due to palliative care being extended to non-cancer illnesses, the collaboration of the professionals from the areas of nephrology and palliative care can have a positive effect on the HRQoL of the patients and their families. Integrating the principles of palliative care into nephrology is beneficial for patients, carers, and professionals (Arnold& Liao, 2006; Noble, Kelly, Rawlings-Anderson, & Meyer, 2007). In this regard, the patient with ACKD could benefit from palliative care on diagnosis of the disease, during RRT stages, and particularly when dialysis is withdrawn, and when conservative kidney management (CKM) is considered (Davison et al., 2015; Leiva-Santos et al., 2012). Thus, this is considered to be a reasonable option for patients with elevated comorbidity, advanced age, and those who do not wish to start dialysis (Brown et al., 2013; Davison et al., 2015).

The lack of studies conducted in Spain prevents comparison of the range of symptoms suffered during the different treatment methods in this culture, and for this reason this aspect needs to be investigated in depth (Gutierrez Sanchez, Leiva-Santos, Sanchez-Hernandez, & Gomez Garcia, 2015). The aims of this study were: (1) to determine the prevalence and severity of symptoms in patients with CKD stage 5 in dialysis and

CKM, and to compare the symptomatology in both groups;(2) to describe the clustering of symptoms;(3) to examine the association between disease severity and symptoms prevalence and severity; and (4) to examine the association between comorbidities and symptoms prevalence and severity.

Theoretical Framework

The study was guided by the theory of unpleasant symptoms (TOUS), which includes the following elements: influencing factors, symptom experience, and consequence (Lenz, Pugh, Milligan, Gift, &Suppe, 1997). This theory emphasizes the multidimensional nature of the symptoms experience. Thus, symptoms are defined not only by their occurrence but also by their level of distress, severity, and frequency. According to this theory symptoms can occur both simultaneously and in isolation. In this regard ACKD patients can experience multiple symptoms, and exploring symptom clustering in this population may improve symptom management.

Methods

Study Design

This study was approved by the Provincial Ethics Committee of Málaga as part of a larger study in which we performed a cross-cultural adaptation and validation of a symptoms assessment tool for patients with ACKD (Gutierrez-Sanchez, Leiva-Santos, Sanchez-Hernandez, Hernandez-Marrero, & Cuesta-Vargas, 2016). All of the data used in this analysis were obtained from a wide sample of patients with CKD stage 4 and 5. In this case we performed a cross-sectional analysis of symptoms, comorbidity and disease severity data in patients with CKD stage 5 in both dialysis and CKM groups. In addition, we explored the association of the symptom prevalence and severity with the level of renal impairment and comorbidities.

Sample

Patients with CKD stage 5 (with an estimated glomerular filtration rate (eGFR) of less than15 mL/min/1.73 m^2) were recruited from the Nephrology Service at Carlos Haya University Hospital in Málaga (Spain), which is a regional teaching hospital with 1,076 beds. All patients were recruited between April and September 2015.

The inclusion criteria were:(1) adult patients with CKD stage 5receiving dialysis or CKM; and (2) Spanish speaking patients. Patients with cognitive impairment and those under the age of 18 years were excluded. In this regard, patients with a diagnosis of dementia (advanced stages) were excluded after reviewing the patients' medical history records.

Measurement

Spanish modified version of POS-S Renal. Symptoms were self-reported by patients using this symptom assessment tool. The original version of this instrument was designed to measure symptoms in patients with ACKD and, it contains 17 symptoms (Murphy, Murtagh, Carey, &Sheerin, 2009). This symptom assessment tool was translated into Spanish. The translation was performed in accordance with the forward and backward method following recommended guidelines, and one symptom was added (cramps) (Muñiz et al., 2013). There were two independent forward translations (English into Spanish). Both versions were compared and, after consensus, 'the preliminary Spanish version of POS-S Renal' was created. This preliminary version was translated back by two native English translators to create, after consensus, a single document. This document was compared with the original to make a consensus document. As a result, a Spanish modified version of this questionnaire that contains 18 symptoms was created. The translation and validation process is reported in a previous study (Gutierrez-Sanchez et al., 2016). This instrument was validated in 200 patients

with CKD stage 4-5 (61 patients were in the dialysis group and 139 patients in the Conservative Kidney Management group). The Spanish modified version of POS-S Renal has been shown to be a reliable and valid instrument to measure symptoms in ACKD (dialysis and CKM) (Gutierrez-Sanchez et al., 2016). In this regard, this questionnaire showed adequate psychometric properties with reference to structural validity, test-retest reliability, and criterion validity (Gutierrez-Sanchez et al., 2016). The exploratory factor analysis (EFA) indicated a two-factor structure of the instrument, and an excellent fit for the two-factor model was obtained with the confirmatory factor analysis (CFA) (comparative fit index = 0.98, root mean square error of approximation= 0.068). The psychometric analysis showed adequate values in terms of reliability to factor 1 (r = 0.909), to factor 2 (r = 0.695), and to total score(r=0.887), internal consistency ($\alpha = 0.78$ to factor 1 and $\alpha = 0.56$ to factor 2), and concurrent validity with a validated instrument that has been used in this population (MSAS-SF)(r=0.860).A symptom severity score can be calculated as a whole, the maximum symptom severity score being 72 (Gutierrez-Sanchez et al., 2016).

eGFR. Data on severity of renal failure were collected using the eGFR, which was calculated using the equation of Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI equation) (Montañés Bermúdez, Bover Sanjuán, Oliver Samper, Ballarín Castán, &Gràcia García, 2010). This equation includes variables such as serum creatinine, age, sex and race to stimate the GFR.

Modified Charlson comorbidity index (mCCI). Comorbidity was collected and scored according to this comorbidity index (Beddhu, Bruns, Saul, Seddon, & Zeidel, 2000). This is a valid comorbidity index that has been widely used, in which each comorbid condition is weighted according to their influence on mortality. The mCCI containts 19 comorbid conditions, which are scored from 1 to 6, and a score of 1

is added for each decade above 40 years. In this modified version, the item of "myocardial infarction" has been replaced from the original version by "cardiovascular disease". A score of 8 or greater is considered as strongly predictive of mortality (Beddhu et al., 2000). Them CCI has not yet been validated for patients with ACKD in CKM although it has been used in this population (Brennan et al. 2015, Yong et al., 2009).

Data Collection Procedures

Potential participants who met the inclusion criteria were selected after reviewing the patients' medical history records.

Patients were recruited and, after receiving information about the project, a written informed consent was obtained. Medical history records and database entries for eligible patients were used to extract information on patient demographics and clinical characteristics, as well as comorbidities. Data on prevalence and severity of symptoms using the POS-S Renal were collected during face-to-face meetings. All data were obtained in the medical consultation and dialysis rooms, from CKM and dialysis patients, respectively.

Data Analysis Procedures

Descriptive analysis was applied to examine demographic and clinical variables. Symptom prevalence was reported using proportions and 95% confidence intervals. Kolmogorov–Smirnov (KS) was performed to determine the sample distribution. The Pearson correlation coefficient was calculated to estimate the relationship between symptoms and disease severity and between symptoms and comorbidity. One-way ANOVA was used for comparison between groups. A p-value of less than 0.05 was taken as statistically significant. Symptom clusters were identified using exploratory factor analysis (EFA). Maximum likelihood extraction (MLE) and Oblimin rotation

were used in EFA. Only the factors with eigenvalues ≥1 were extracted. For factor loading, symptoms were considered to be loaded on a factor if the factor loading was ≥0.50. Kaiser–Meyer–Olkin (KMO) values and Bartlett's test of Sphericity were used to evaluate the factorability of the data.

Intraclass correlation coefficient type 2.1 (two-way mixed effects model) ($ICC_{2.1}$), was used to calculate Cronbach's α coefficients and to evaluate internal consistency (Cronbach, 1951). This analysis was performed using statistical analysis software SPSS version 20.

Results

Sample Characteristics

A total of 123 patients with CKD stage 5, including 63 patients in the CKM group, and 60 patients in the dialysis group (47 patients on hemodialysis and 16 patients on peritonal dialysis), participated in this study. The sociodemographic and clinical characteristics are shown in Table 1. The missing values do not exceed 2%. The mean ± SD score for the mCCI was 5.6 ±2.5 for the total sample. Diabetes, tumor, coronary artery disease, congestive heart failure, and peripheral vascular disease, were the main comorbid conditions of these patients. No significant differences were found for comorbidities conditions between groups. The mCCI scores are shown in Table 2.

Table 1. *Sociodemographic and Clinical Characteristics of the Sample (N=123)*

Characteristics	**Total (N=123)**	**Conservative Managementgroup(n=63)**	**Dialysis group (n=60)**	**P**
Age (mean, SD)	63.3 (±14.7)	67.4 (±12.6)	58.9 (±15.5)	0.001
Gender				0.343

Male	75 (61%)	41 (65.1%)	34 (56.7%)	
Female	48 (39%)	22 (34.9%)	26 (43.3%)	
Ethnicity				
Caucasian	123 (100%)	63 (100%)	60 (100%)	
Spanish descent	117 (95.1%)	57 (90.4%)	60 (100%)	
British descent	3 (2.4%)	3(4.7%)	0 (0%)	
German descent	3 (2.4%)	3(4.7%)	0 (0%)	
Marital status				0.498
Married	84 (68.3%)	44 (69.8%)	40 (66.7%)	
Not married	39 (31.7%)	19 (30.2%)	20 (33.3%)	
Disease severity in eGFR, ml/min (mean, SD)	9.1 (±3.4)	11.3 (±2.3)	6.8 (±2.7)	<0.001
Months in RCM or dialysis (mean, SD)	32.1 (±31.3)	25.9 (±19.8)	38.6 (±39.1)	0.025
Causes of CKD				0.061
Renal vascular disease	37 (30.1%)	27 (42.9%)	10 (16.7%)	

Diabetic nephropathy	19 (15.4%)	9 (14.3%)	10 (16.7%)	
Primary glomerular disease	13 (10.6%)	5 (7.9%)	8 (13.3%)	
Polycystic kidneys	11 (8.9%)	6 (9.5%)	5 (8.3%)	
Unknown aetiology	16 (13%)	10 (15.9%)	6 (10%)	
Others	27 (21.9%)	6 (9.5%)	21 (35%)	

Prevalence and Severity of Symptoms

The most prevalent symptoms reported (ranges in values for both groups combined) were weakness — 78.7% (CI: 72–87%), pain — 55.3% (CI: 46–65%), difficulty sleeping — 54.5% (CI: 47–66%), feeling depressed — 50.4% (CI:41–60%), mouth problems — 45% (CI: 36–54%), changes in skin — 46.3% (CI: 35–54%), poor appetite — 41.5% (CI: 30–49%), poor mobility — 41.3%(CI: 32–51%), drowsiness — 39.5 %(CI: 31–50%), feeling anxious — 37.7% (CI: 28–47%), itching — 36.1% (CI: 28–47%), and shortness of breath — 32.8% (CI: 23–41%).

No significant difference for the prevalence of symptoms was found between CKM and dialysis groups, except for lack of appetite, which was more prevalent in the CKM group (p=0.012). The comparison of symptom prevalence between KCM and dialysis groups is shown in Figure 1. The number of symptoms reported by the total sample was 0 to 15 per patient, the mean number of symptoms reported being 6.5 (SD ±3.4) from a maximum of 18. The mean symptom severity score was 11.7 (SD±7.6) and the mean severity score of each symptom was 1.8 (slight severity). The most intense

symptoms (from severe to overwhelming) were: pain (22%), weakness (19%), itching (14%), poor mobility (9%), difficulty sleeping (8%), and constipation (8%).

Table 2. *Modified Charlson Comorbidity Index and Prevalence of Comorbid Conditions (N=123)*

Condition	**Total (N=123)**	**Conservative management group (n=63)**	**Dialysis group (n=60)**	**P**
Coronary artery disease	21 (17.1%)	11 (17.5%)	10 (16.7%)	
Congestive heart failure	16 (13%)	9 (14.3%)	7 (11.7%)	
Peripheral vascular disease	11 (8.9%)	4 (6.3%)	7 (11.7%)	
Cerebrovascular disease	6 (4.9%)	2 (3.2%)	4 (6.7%)	
Dementia	0 (0%)	0 (0%)	0 (0%)	
Chronic pulmonary disease	7 (5.7%)	3 (4.8%)	4 (6.7%)	
Connective tissue disease	7 (5.7%)	4 (6.3%)	3 (5%)	
Peptic ulcer disease	7 (5.7%)	3 (4.8%)	4 (6.7%)	
Mild liver disease	7 (5.7%)	2 (3.2%)	5 (8.3%)	
Diabetes mellitus	9 (7.3%)	6 (9.5%)	3 (5%)	
Hemiplegia	0 (0%)	0 (0%)	0 (0%)	
Moderate or severe renal disease	123 (100%)	123 (100%)	123 (100%)	
Diabetes with end organ damage	26 (21.1%)	15 (23.8%)	11 (18.3%)	
Any tumor, leukemia, lymphoma	22 (17.9%)	12 (19%)	10 (16.7%)	
Moderate or severe liver	1 (0.8%)	1 (1.6%)	0 (0%)	

disease				
Metastatic solid tumor	2 (1.6%)	0 (0%)	2 (3.3%)	
AIDS	0 (0%)	0 (0%)	0 (0%)	
CCI score (mean, SD)	5.6 (±2.5)	5.8 (±2.2%)	5.3 (±2.7)	0.238

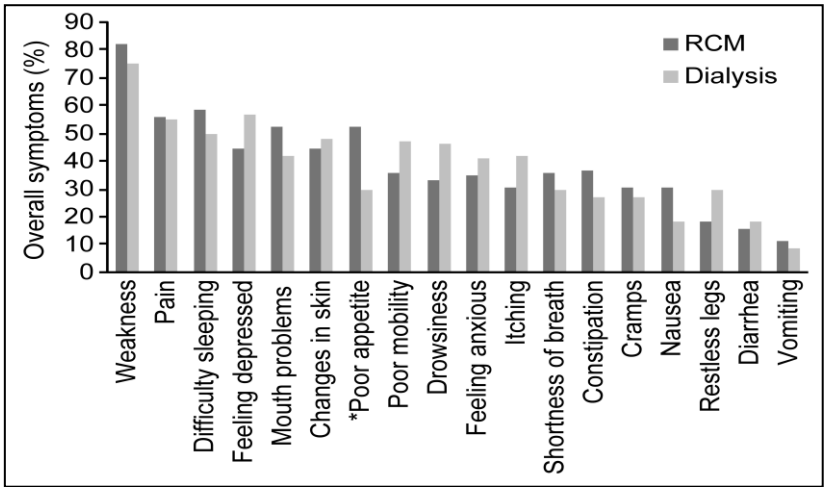

Figure 1. *Comparison of symptom prevalence between CKM and dialysis groups.*

Note. Difference between groups: *p<.05

Symptom Clusters

Data factorability was determined as suitable from the KMO value of 0.699 and a highly significant Bartlett's Test of Sphericity ($p < 0.001$). The factor analysis revealed an initial solution with seven factors with an eigenvalues greater than 1 and 68.17% of the variance. However, the scree plot showed a two-factor solution and only 35.43% of the variance was explained with two factors, an eigenvalue higher than 1, and 11.3% of variance explained (Figure 2). The results of the rotated components matrix are shown in Table 3. Two symptom clusters were identified. Cluster 1 included

weakness, mouth problems, poor mobility, difficulty sleeping, feeling anxious, and feeling depressed, and these comprised the largest proportion of the total variance (24.13%). Cluster 2 included nausea, vomiting, and diarrhea and contributed 11.3% of the total variance.

The internal consistency was good for cluster 1 (Cronbach's alpha coefficient = 0.745, with values ranging from 0.667 to 0.810) and moderate for cluster 2 (Cronbach's alpha coefficient =0.674, with values ranging from 0.560 to 0.762) (Cronbach, 1951).

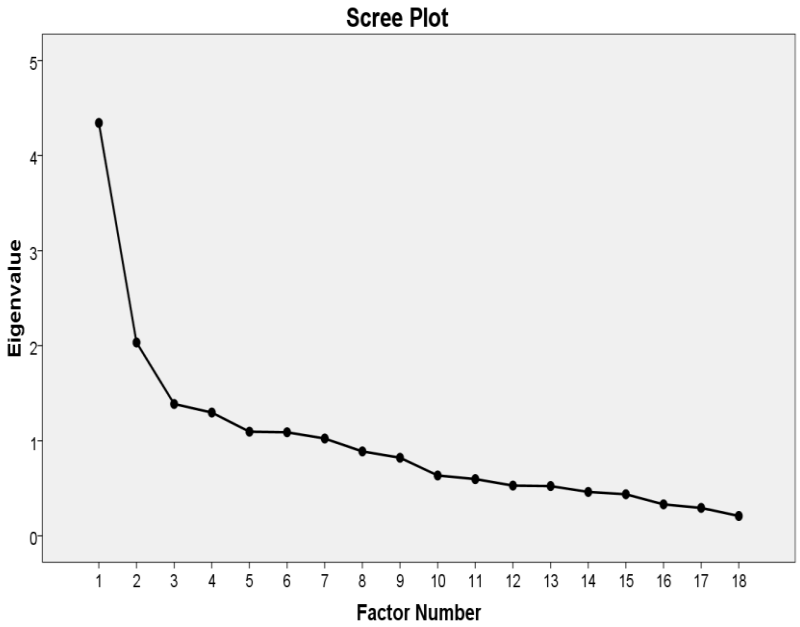

Figure 2. *Screeplot of the exploratory two factor solution*

Association Between Disease Severity and Symptoms

We evaluated the effect of the level of renal failure (disease severity) on symptom burden (global score, number, and severity of symptoms). The results showed that there was no statistical significant correlation between the disease severity and the global symptom score (r=0.958 for the total sample population, r=0.262 for the dialysis group, and r=0.324 for the CKM group), between disease severity and the number of reported symptoms (r=0.891 for the total sample population, r=0.649 for the dialysis

group, and r=0.424 for the CKM group), and between disease severity and the symptoms severity (r=0.334 for the total sample population, r=0.718 for the dialysis group, and r=0.439for the CKM group).

Table 3. *Factor loading of oblimin rotated factor pattern*

Item	**Factor 1**	**Factor 2**
Pain	0.439	-0.140
Shortness of breath	0.400	-0.373
Weakness or lack of energy	**0.538**	-0.362
Nausea	0.199	**-0.842**
Vomiting	0.175	**-0.697**
Poor appetite	0.486	-0.229
Constipation	0.309	-0.017
Mouth problems	**0.624**	-0.265
Drowsiness	0.438	-0.276
Poor mobility	**0.651**	-0.041
Itching	0.275	-0.211
Difficulty sleeping	**0.570**	-0.351
Restless legs	0.178	-0.241
Feeling anxious	**0.556**	-0.214
Feeling depressed	**0.603**	-0.106
Changes in skin	0.363	-0.337
Diarrhea	0.205	**-0.548**
Muscle cramps	0.147	-0.342

Notes. Extraction Method: Maximum Likelihood. Rotation Method: Oblimin with Kaiser Normalisation.Suppression at 0.5

Association Between Comorbidities and Symptoms

The effect of the comorbidities on symptom burden was also evaluated. The results indicated that there was no statistical significant correlation between comorbidities and the global symptom score (r=0.470 for the total sample population, r=0.926 for the dialysis group, and r= 0.298 for the CKM group), between comorbidities and the number of symptoms reported (r=0.79for the total sample population and r=0.608for the dialysis group), and between comorbidities and the severity of symptoms reported (r=0.393 for the total sample population, r=0.485 for the dialysis group, and r= 0.752 for the CKM group). There was, however, a significant correlation between comorbidities and the number of reported symptoms in the CKM group.

Discussion

To our knowledge, this is the first study to be conducted in Spain that explores the symptom burden clusters in patients with CKD stage 5 on dialysis and CKM. The symptomatology of patients with ACKD on dialysis and CKM has been widely studied (Murtaghet al., 2007; O'Connor& Kumar, 2012). Several factors such as kidney failure (pruritus and restless legs syndrome), the associated comorbidity (diabetic neuropathy, angina, etc.), or the factors associated with the RRT (cramps, problems with sleeping related to nocturnal alarms during PD), can have an influence on the symptomatology (Brown et al., 2013). In addition, symptoms in CKD occur in clusters rather than in an isolation way (Almutary et al., 2016; Jablonsky, 2007). In this regard, symptom cluster research in ACKD is beginning to emerge, with symptom burden and cluster being an area of special interest in CKD (Almutary et al., 2016; Jablonsky, 2007).

Our data reinforce the conclusion of other studies that patients with CKD stage 5 experience not only a high symptom burden, but also a wide range of symptoms

(Murtagh et al., 2007; O'Connor& Kumar, 2012). In addition, these patients have a high level of comorbid conditions. In this regard, there is an increase in the number of elderly patients, many with multiple comorbidities, commencing dialysis, with dialysis therapies in the elderly being associated with functional status decline. Furthermore, the quantity and chronicity of the consumption of medications in this population is high. In consequence, kidney failure, comorbid conditions and chronicity of the consumption of medications, dialysis, or several of these components working together, can contribute to the symptoms reported in the POS-S Renal (Murtagh et al., 2007, Brown et al., 2013). The results indicate that the prevalence of symptoms was similar in both CKM and dialysis groups, although we found a significant difference between the groups for lack of appetite, which was more prevalent in the CKM group($p=0.012$). Over half of the patients described weakness, pain, difficulty sleeping, and feeling depressed; weakness and pain being among the most intense symptoms. These symptoms are consistent across studies of ACKD patients and they are associated with lower HRQoL (Murtagh et al., 2007; O'Connor& Kumar, 2012).

Weakness is a prevalent symptom in ACKD that is associated with global symptom burden, suggesting that an adequate management of symptom clusters with a multidimensional approach may reduce this symptom (Almutary et al., 2016; Murtagh et al., 2007; O'Connor& Kumar, 2012). Several factors, such as sleep disorders, depression, anemia, RRT, and renal disease itself have an influence on this symptom (Zalai & Bohra, 2016). Our results indicate that weakness was the most prevalent symptom in this sample population. No significant difference between the two groups was found ($p=0.332$), although this symptom was more prevalent in the CKM group. Energy conservation and other rehabilitative interventions can be effective to improve management of this symptom.

Pain is a significant problem in this population. The causes of pain in ACKD patients are diverse and are associated with peripheral neuropathy, peripheral vascular, or musculoskeletal problems (Davison, 2003). Evidence shows that this symptom is associated with greater insomnia and depressive symptoms (Davison & Jhangri 2010, Davison, Koncicki, & Brennan, 2014). In our study pain was the second most prevalent symptom.

Sleep disorders (sleep apnea, insomnia, restless legs syndrome, and excessive daytime sleepiness) are common in ACKD and they are interconnected with other symptoms such as weakness and depression (Araujo et al., 2011;Brekkeet al., 2013; Iliescu, Yeates, & Holland, 2004; Sabbatini et al., 2002;Stepanski, Faber, Zorick, Basner, & Roth, 1995).Several factors, such as psychological disorders (depression and anxiety), lifestyle, treatment, and comorbidities, can have an influence on these disorders (Maung, El Sara, Chapman, Cohen, & Cukor, 2016). In our study difficulty in sleeping was one of the most intense symptoms and this was more common in the CKM group.

Patients receiving dialysis, experience multiple emotional symptoms and, particularly, a high prevalence of depression, which is associated with poor HRQoL, physical, and emotional symptoms (Abdel-Kader et al., 2009; Son, Choi, Park, Base, & Lee, 2009; Weisbord et al., 2005). RRT has an impact on physical and psychosocial well-being and it results in a significant change in the lifestyle for many patients. In this regard, the results of our study show that depression was more frequent in the dialysis group, although no significant difference was found between groups (p=0.178). This suggests the need for a multidimensional approach with an adequate psychological intervention for this population.

In contrast to prior studies that have focused on hemodialysis patients (Jablonski 2007; Yu, Huang, & Tsai, 2012), we specifically explored symptom clusters in a cohort of patients with CKD stage 5 receiving dialysis and non-dialysis treatment. The sample size was adequate for the factor analysis, with a KMO value of 0.699 (Polit & Beck. 2004). Based on the factor analysis, two clusters were identified. The internal consistency was good for cluster 1 ($\alpha = 0.745$) and moderate for cluster 2 ($\alpha = 0.674$), which indicates a satisfactory degree of interrelatedness among the symptoms (Cronbach, 1951). Cluster 1 was related to neuropsychological symptoms and these included weakness, mouth problems, poor mobility, difficulty sleeping, feeling anxious, and feeling depressed. A similar cluster categorized as "cluster of energy and sensory discomfort" has been reported in a previous study (Yu et al., 2012). Cluster 2 was related to gastrointestinal symptoms, and these included nausea, vomiting, and diarrhea. Gastrointestinal clusters have been reported in other studies (Almutary et al., 2016; Jablonski, 2007). In contrast to the widespread prevalence of the gastrointestinal cluster, cluster 1 has not been totally reproduced in other studies. One possible explanation is that most of the previous studies used a different instrument to explore the burden of symptoms, and did not include both groups (dialysis and non-dialysis treatment). The tendency of these symptoms to occur together has implications for the development of appropriate interventions to improve symptom management in this population. In this regard, interventions such as individualized exercise regimens and a psychoeducational approach to managing weakness, anxiety, difficulty sleeping, and depression, targeted at the symptom cluster level, can be effective (Almutary, Douglas, & Bonner, 2017). This is especially important for symptoms such as anxiety and depression, which can reduce treatment adherence in ACKD (Almutary et al., 2017). Thus, these interventions need to

be incorporated in nursing care plans to reduce the impact of symptoms in this population.

Patients with ACKD receiving dialysis or CKM, are highly burdened with symptoms regardless of the level of eGFR. Our results reinforce this, indicating that there was no significant correlation between the disease severity and the number, severity, and global score of symptoms. These results were comparable to those found by the authors of other studies (Brennan, Collett, Josland, & Brown, 2015; Murphy et al., 2009).

Concerning the association between comorbidities and the severity and global symptom score, no significant correlation was found, although a significant correlation between comorbidities and the number of symptoms reported in CKM group was found. These findings were comparable to those found by Murphy and colleagues who found that there was a trend towards a significant difference between comorbidities and the number of symptoms reported (Murphy et al., 2009).

Previous studies indicate that the symptoms experienced in ACDK are similar to those found in the terminal stages of other illnesses, such as advanced cancer, congestive heart failure, chronic obstructive pulmonary disease, and AIDS (Janssen, Spruit, Wouters, & Schols, 2008; Solano, Gomes, & Higginson, 2006). Symptoms such as pain, fatigue, breathlessness, insomnia or depression are highly prevalent in these illnesses, indicating that a common pathway of symptoms is experienced towards the end of life (Janssen et al., 2008; Solano et al., 2006). This suggests that palliative care can be relevant for improving the quality of care, HRQoL, and symptoms management in these patients. Hence, palliative care principles need to be integrated into the routine care of patients with ACKD (Tamura & Meier 2013). This is especially important in

Spain, where the integration of palliative care principles in nephrology services is suboptimal, negatively affecting the global patient outcomes.

This study shows the value of routine assessment of symptoms in ACKD. In this regard, patient report outcome measure (PROMs) allows the clinician to evaluate and monitor the wide range of symptoms experienced by these patients. This is especially important in ACKD where PROMs can be used by nurses to assess and facilitate the introduction of interventions (Perrone, Coons, Cavanaugh, Finkelstein, & Meyer, 2013). In addition, it is useful to have instruments that can be used in dialysis and CKM populations in order to better monitor the symptoms of the patients as they progress through CKD stages. Hence, standardization of symptoms assessment tools can be useful in both clinical and research settings (Gutierrez-Sanchez et al., 2016).

There are some limitations in this study. This is a cross-sectional study and symptoms can change as disease progresses. Our results may not be generalizable because the cohort does not represent the broader population of patients with CKD stage 5in dialysis and CKM. Furthermore, this study was only conducted in one center. Further longitudinal studies are needed that use a wider sample population and explore symptom burden as disease progresses.

Implications for Practice

The results from this study indicate the need for routine assessment of symptoms in ACKD. Patients with CKD stage 5, experience multiple symptoms that negatively affect the quality of life (Abdel-Kader et al., 2009; Iyasere & Brown, 2014). The tendency of these symptoms to occur together has implications for the development of interventions to improve symptom management in this population (Almutary et al., 2016; Jablonsky, 2007). Further work is needed that investigates the effectiveness of interventions on symptom management.

Conclusions

Patients with CKD stage 5 have a significant burden of symptoms. The symptom prevalence overlapped considerably in both groups of patients (dialysis and CKM), with weakness, pain, difficulty sleeping, and feeling depressed being the most prevalent symptoms in both groups.

The pattern of symptom clusters in CKD stage 5 has a clinical relevance and clinical interventions should be designed to address these clusters in order to improve symptom management in this population. In this regard, interventions targeted at the symptom cluster level need to be incorporated in nursing care plans. The integration of palliative care in nephrology services is urgently required to optimize the care of this population.

The results emphasize the need to assess and monitor the wide range of symptoms in ACKD to provide better management of the symptomatology. In this regard, the utility of routine symptoms assessment is reinforced in this study.

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