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Authors
Lockwood, Mark B
Lash, James P
Pauls, Heather
et al.

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Physical Symptom Cluster Subgroups in Chronic Kidney Disease

Mark B. Lockwood, PhD, MSN, RN [Assistant Professor],
Department of Biobehavioral Health Science, University of Illinois at Chicago.

James P. Lash, MD [Professor of Medicine],
Division of Nephrology, University of Illinois at Chicago College of Medicine.

Heather Pauls, MPH [Visiting Research Specialist],
Department of Health System Science, University of Illinois at Chicago.

Seon Yoon Chung, PhD, RN [Associate Professor],
Illinois State University Mennonite College of Nursing, Normal.

Manpreet Samra, MD [Assistant Professor of Clinical Medicine],
Division of Nephrology, University of Illinois at Chicago College of Medicine.

Catherine Ryan, PhD, APN, CCRN-K, FAHA, FAAN [Clinical Associate Professor],
Department of Biobehavioral Health Science, University of Illinois at Chicago.

Chang Park, PhD [Research Assistant Professor/Senior Biostatistician],
Department of Health System Science, University of Illinois at Chicago.

Holli DeVon, PhD, RN, FAHA, FAAN [Professor and Associate Dean for Research],
University of California, Los Angeles School of Nursing.

Ulf G. Bronas, PhD, ATC, FAHA [Associate Professor]
Department of Biobehavioral Health Science, University of Illinois at Chicago.

Abstract

Background: Symptom burden associated with chronic kidney disease can be debilitating, with a negative effect on patient health-related quality of life. Latent class clustering analysis is an innovative tool for classifying patient symptom experience.

Objectives: The aim of the study was to identify subgroups of patients at greatest risk for high symptom burden, which may facilitate development of patient-centered symptom management interventions.

Methods: In this cross-sectional analysis, baseline data were analyzed from 3,921 adults enrolled in the Chronic Renal Insufficiency Cohort Study from 2003 to 2008. Latent class cluster modeling using 11 items on the Kidney Disease Quality of Life symptom profile was employed to identify patient subgroups based on similar observed physical symptom response patterns. Multinomial

Corresponding author: Mark B. Lockwood, PhD, MSN, RN, University of Illinois at Chicago College of Nursing, 845 South Damen Ave. (MC 802), Chicago, IL 60612-7350 (lockmar@uic.edu).

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logistic regression models were estimated with demographic variables, lifestyle and clinical variables, and self-reported measures (Kidney Disease Quality of Life physical and mental component summaries and the Beck Depression Inventory).

Results: Three symptom-based subgroups were identified, differing in severity (low symptom, moderate symptom, and high symptom). After adjusting for other variables in multinomial logistic regression, membership in the high-symptom subgroup was less likely for non-Hispanic Blacks and men. Other factors associated with membership in the high-symptom subgroup included lower estimated glomerular filtration rate, history of cardiac/cardiovascular disease, higher Beck Depression Inventory scores, and lower Kidney Disease Quality of Life physical and mental component summaries.

Discussion: Three symptom subgroups of patients were identified among patients with mild-to-moderate chronic kidney disease. Several demographic and clinical variables predicted membership in subgroups. Further research is needed to determine if symptom subgroups are stable over time and can be used to predict healthcare utilization and clinical outcomes.

Keywords

kidney disease; latent class analysis; quality of life

Better understanding the effects of symptom burden on patient outcomes among patients with chronic kidney disease (CKD) has been identified as a priority by the Kidney Health Initiative, a public-private partnership between the Food and Drug Administration and the American Society of Nephrology (Flythe et al., 2019). Progression of kidney disease is often insidious, and many sentinel symptoms associated with CKD go unnoticed until the disease has progressed to late stages. Late stages of CKD are characterized by significant symptom burden, resulting in poor quality of life (QoL), loss of productivity related to disability, and significant morbidity and mortality (Porter et al., 2016). Patients in advanced stages of disease experience multiple co-occurring symptoms (Almutary, Bonner, & Douglas, 2013). Symptom burden associated with end-stage renal disease (ESRD) is similar to that experienced by patients with terminal cancer (Saini et al., 2006). From the patient perspective, reduction of symptoms is more important than prolongation of life. Ramkumar, Beddhu, Eggers, Pappas, and Cheung (2005) found in a study of patients with ESRD that 94% receiving hemodialysis as renal replacement therapy reported that they would accept additional dialysis sessions if it would reduce their symptom burden, while only 19% said they would endure additional dialysis treatments to extend their survival (Ramkumar et al., 2005). Currently, there is a paucity of evidence related to symptom burden and patient outcomes in mild-to-moderate CKD. Thus, better understanding the implications of symptom burden is important to improving patient-centered care in this growing population.

Evidence is emerging that symptoms experienced in chronic disease often present as co-occurring symptoms, also known as symptom clusters (Miaskowski et al., 2015). A symptom cluster is generally defined as groups of two or more concurrent symptoms that relate to one another and are independent of other symptom clusters (Dodd, Miaskowski, & Lee, 2004; Kim, McGuire, Tulman, & Barsevick, 2005). Key to the concept of the symptom cluster is the premise that symptom clusters may share a common biological etiology; thus,

resolution of one symptom may have synergistic effects on related symptoms (Kim et al., 2005). Variable-centered approaches to clustering, which seek to identify relationships among symptoms and quantify the patient's symptom experience, have been employed in patients with ESRD (Amro et al., 2015; Yu, Huang, & Tsai, 2012). Fatigue (Jhamb et al., 2013; Rodrigue et al., 2011), sleep disturbance (Nigam, Camacho, Chang, & Riaz, 2018), depression/anxiety (Assari & Burgard, 2015), pain (Song, Paul, Ward, Gilet, & Hladik, 2018), and gastrointestinal symptoms (Zhang, Bansal, Go, & Hsu, 2015) are among the most common co-occurring symptoms in CKD (Lockwood et al., 2019). Although variable center approaches are useful in examining relationships among homogeneous populations (Conley, 2017), variable-centered approaches to clustering symptoms are complicated by difficulty interpreting symptom clusters due to heterogeneity of symptom response patterns, thereby limiting their clinical utility (Conley, 2017; Lockwood et al., 2019; Ryan et al., 2019).

Latent class analysis (LCA), a person-centered clustering approach, classifies subgroups of people based on similar symptom response patterns and has emerged as a powerful tool in assessing the effect of symptom experience on patient outcomes in heterogeneous populations (Conley, 2017; Ryan et al., 2019). Person-centered symptom clustering has been successfully employed in oncology (Miaskowski et al., 2015), cardiovascular disease (Ryan et al., 2019), and ESRD (Almutary, Douglas, & Bonner, 2017). Despite these advancements, little is known about person-centered symptom clustering in mild-to-moderate CKD. The present study aims to address this gap.

The purpose of this study was to use baseline data from the Chronic Renal Insufficiency Cohort and Hispanic Chronic Renal Insufficiency Cohort (CRIC) studies to identify latent classes (in this case, symptom subgroups) of individuals with mild-to-moderate CKD. The research question was: At baseline, will participants with mild-to-moderate kidney disease cluster into distinct subgroups based on self-reported symptom data from the Kidney Disease Quality of Life (KDQOL-36) symptom profile? Therefore, the latent classes were determined based on similar symptom response patterns ascertained from the baseline KDQOL-36 symptom profiles. We hypothesized that we could classify subgroups of patients with similar symptom experiences and that subgroup membership would differ by age, gender, race/ethnicity, and clinical measures of kidney function.

METHODS

Study Population

This was a cross-sectional, exploratory analysis of baseline data from the prospective CRIC Study. The study design and baseline characteristics of participants have been described previously (Feldman et al., 2003; Lash et al., 2009). In brief, the CRIC Study enrolled a demographically and clinically heterogeneous group of participants aged 21–74 years with CKD. CKD was determined by an age-based estimated glomerular filtration rate (eGFR) of 20–70 ml/min/1.73 m^2. In total, 3,939 participants were enrolled in the primary study between May 2003 and June 2008 from seven clinical centers in the United States. Data collected at the baseline visit included a physical examination, medical history, demographic information, and medication history. Detailed inclusion/exclusion criteria can be found elsewhere (Lash et al., 2009). Briefly, the CRIC Study included a racially and ethnically

diverse group of adult patients aged 21–74 years with mild-to-moderate CKD. Nearly half of the participant had diabetes. Age-based eGFR entry criteria were established to limit the proportion of older individuals who were recruited with age-related diminutions of GFR but otherwise nonprogressive CKD. Patients with polycystic kidney disease and those with kidney disease requiring immunosuppression were excluded, as were patients with significant comorbidities (Lash et al., 2009). Institutional review board approval was received from each of the seven centers participating in the primary CRIC Study. The study was conducted in compliance with the Declaration of Helsinki. Written informed consent was obtained from all participants in the primary study. The institutional review board at the University of Illinois at Chicago approved the secondary analysis presented here.

Outcome

In the present analysis, we used LCA to identify symptom subgroups of patients based on 11 items contained in the KDQOL-36 symptom profile (Hays, Kallich, Mapes, Coons, & Carter, 1994). Symptoms included itchy skin, dry skin, muscle soreness, feeling washed out or drained, shortness of breath, chest pain, lack of appetite, numbness in the hands and feet, nausea or upset stomach, cramps, and faintness/dizziness. The symptoms were measured using a Likert-type scale that measured the extent to which the participant was bothered by the symptom in the past 4 weeks (*not at all bothered, somewhat bothered, moderately bothered, very much bothered*, and *extremely bothered*). The KDQOL-36 is the most frequently used health-related QoL (HRQoL) instruments in kidney disease and has proven construct validity and adequate to excellent internal reliability (Hays et al., 1994).

Covariates

Six demographic variables were considered in bivariate models: race, age, income, marital status, education, and gender. In addition, seven health/clinical characteristics were considered: smoking habit, kidney function (modeled as continuous eGFR), presence or absence of self-reported cardiovascular events history (myocardial infarction, peripheral vascular disease, congestive heart failure, atrial fibrillation, and stroke), body mass index (BMI), hypertension, and diabetes. Hypertension was defined as systolic blood pressure of >140 mm Hg, diastolic blood pressure of ≥ 90 mm Hg, or use of antihypertensive medications. Diabetes was defined as fasting blood glucose of ≥126 mg/dl or the use of oral hypoglycemic medications or insulin. HRQoL was evaluated using the KDQOL-36 (Assari & Burgard, 2015), which includes 43 kidney disease-specific items divided into domains, including symptoms/problems, effects of kidney disease, burden of kidney disease, work status, cognitive function, quality of social interaction, sexual function, sleep, social support, staff encouragement, and patient satisfaction. Higher scores indicate a higher level of HRQoL. Depressive symptoms were assessed using the Beck Depression Inventory (BDI), which is a 21-item depression questionnaire with cutoff scores among the general population indicating depressive symptom severity: <9 = *no depressive symptoms*, 10–15 = *mild depressive symptoms*, 16–23 = *moderate depressive symptoms*, and >24 = *severe depressive symptoms* (Beck, Steer, & Carbin, 1988). Of note, Hedayati, Minhajuddin, Toto, Morris, and Rush (2009) identified a BDI score of >11 as a sensitive and specific cutoff value for identifying major depressive symptoms among patients with CKD not yet on dialysis (Hedayati et al., 2009).

Statistical Analysis

For the purpose of the current analysis, LCAhas several advantages compared to commonly used variable-centered clustering techniques such as principal component analysis. First, the primary purpose of LCA is to identify unobservable subgroups from the data—in this case, symptom subgroups. LCA is model-based and generates probabilities of membership into subgroups. Second, LCA employs statistical fit indices to allow assessment of how well the data fit the model. Finally, LCA has been used to identify patient subgroups with similar symptom response patterns in several clinical studies in oncology (Kim, Abraham, & Malone, 2013), cardiovascular disease (Ryan et al., 2019), and chronic illness (Miaskowski et al., 2015). Thus, using LCA to identify an otherwise unobservable variable—physical symptom subgroups among patients with mild-to-moderate CKD—may provide a more clinically meaningful variable to be included in patient-centered intervention studies aimed at determining the moderating effect of symptoms on important patient outcomes.

LCA—as a model-based cluster method—was applied to classify participants into subclasses with similar physical symptom response patterns from the KDQOL-36 symptom profile. The optimal number of subgroups was determined by minimum information criteria, such as Bayesian information criterion and maximum entropy statistics. The statistical significance of model difference of different cluster numbers was determined by using the Vuong-Lo-Mendell-Rubin adjusted likelihood ratio test (Nylund, Asparouhov, & Muthén, 2007). To improve maximum likelihood estimation, initial stage random starts were set at 20. Chi-square and one-way analysis of variance tests were conducted to determine if a symptom subgroup was associated with individual patient characteristics.

Multinomial logistic regression (MLR) modeling estimated the likelihood of membership in the high-symptom subgroup compared to the low-symptom subgroup. Independent variables in MLR were selected by their status as historically important clinical variables of CKD severity. Variables selected for the model were gender, race/ethnicity, annual household income, educational attainment, continuous age, smoking status, continuous eGFR, continuous BMI, systolic and diastolic blood pressure, diabetes status, cardiovascular history (congestive heart failure, atrial fibrillation, peripheral arterial disease, stroke, and myocardial infarction, categorized as *yes* vs. *no/do not know*), KDQOL-36 physical component score (PCS) and mental component score (MCS), and continuous BDI score. Significance levels were determined at $p \leq .05$. LCA was estimated using Mplus V 8.1 (Muthén & Muthén, 2018); all other analyses were conducted in StataIC 15 (StataCorp., College Station, TX).

RESULTS

The final sample for symptom clustering included 3,921 participants with nonmissing symptom data (18 participants were excluded because they were missing all symptom data on the KDQOL-36). There were no significant differences between individuals with missing symptom data and those included in the analyses. The mean age of the sample was 58 (±11) years (Table 1). The sample was racially/ethnically heterogeneous, and there were slightly more men than women (55% vs. 45%). More than half of the sample reported making under $50,000 per year, and 40% reported an education of high school or less. Half of the

participants reported diabetes, and 87% reported a history of hypertension. The mean eGFR was 41 (±11) ml/min/1.73 m^2 (Table 1).

Symptom subgroups were evaluated using self-reported severity of physical symptoms from the KDQOL-36 (Figure 1). Initially, the minimum Bayesian information criterion LCA model was identified as a six-cluster model; however, entropy statistics indicated a three-cluster model as the appropriate model (Table 2). To determine subgroups with a more robust method, the Vuong-Lo-Mendell-Rubin likelihood ratio test and the Lo-Mendell-Rubin adjusted likelihood ratio test were applied. The likelihood ratio test results indicated a four-cluster model. However, the fourth component of the four-cluster model consisted of the 18 subjects missing symptom item profile. Therefore, the fourth cluster was excluded from this study. The three symptom subgroups determined from LCA were labeled low symptom subgroup, moderate symptom subgroup, and high symptom subgroup.

MLR models were constructed to identify predictors of cluster membership (Table 3). Diabetes status was included as a covariate in MLR models because the primary study purposefully sampled 50% of participants to have a history of diabetes. Ultimately, 3,791 participants (96% of the original sample) were analyzed in the MLR due to missing data on the covariates on 130 participants. Because the number of participants with missing data was less than 5%, exclusion of these subjects from the MLR should not bias the analysis. Compared to non-Hispanic Whites, non-Hispanic Blacks had a 37% lower risk for membership in the high versus low symptom subgroup when controlling for all other variables in the model. A similar result was seen in the diabetic group, but not in the nondiabetic group. Compared to women, men had a lower risk for membership in the high versus low symptom subgroup. The relative risk for membership into the high symptom subgroup among men would be expected to decrease by 38%. Kidney function was a significant predictor of symptom subgroup membership. For every 10 ml/min/1.73 m^2 unit increase in eGFR, the risk of membership in the high versus low symptom subgroup decreased by 20%.

Individuals with congestive heart failure had a 67% increased risk of membership in the high versus low symptom subgroup as compared to individuals without heart failure. The risk increased more than twofold among those with heart failure and concomitant diabetes (data not shown). Individuals with atrial fibrillation and peripheral artery disease had a 65% and 79% increased risk of membership in the high versus low symptom subgroup, respectively, as compared to individuals without. Individuals with a history of stroke had a 35% decreased risk of membership in the high versus low symptom subgroup, respectively, as compared to individuals with no history. However, the number of individuals with a history of stroke was small ($n = 390$).

Self-reported BDI scores and PCS and MCS scores from the KDQOL-36 predicted subgroup membership in all analyses. For every 1 point higher BDI score, the risk for membership in the high versus low symptom group grew 13% higher. For every one-unit increase on the KDQOL-36 PCS score, the risk for membership in the high versus low symptom subgroup was 15% lower. For every one-unit increase in the KDQOL-36 MCS score, the risk for membership in the high symptom subgroup was 12% lower. A graded

decrease in KDQOL-36 subscales was noted from high to low symptom subgroups (Figure 2).

DISCUSSION

This study provides valuable insight into the potential role of person-centered symptom clustering in patients with CKD and a novel use of data from the KDQOL-36 beyond assessment of HRQoL. We used LCA to identify symptom subgroups based on symptom severity response patterns in a large, heterogeneous population of patients with mild-to-moderate CKD (Stages 2–4). We identified three distinct symptom subgroups (high, moderate, and low) that were associated with several demographic and clinical variables. Determining unique characteristics of the symptom subgroups by exploring associations between a combination of demographic and clinical variables and similar observed physical symptom response patterns may provide a clinically useful tool to identify patients at greater risk of adverse clinical and health utilization outcomes using data that are otherwise unobservable. However, longitudinal analyses are needed to determine if symptom subgroups can predict groups at greater risk of poor outcomes.

Moderate-to-severe depression is common among patients with ESRD (Alavi, Aliakbarzadeh, & Sharifi, 2009). In the current analysis, we found that the mean scores on the BDI were fourfold higher among patients in the high symptom subgroup compared to the low symptom subgroup. The mean score on the BDI in the high symptom subgroup was 16.8—well above the cutoff score of ≥11 previously identified as a predictor of major depressive symptoms among CKD patients not yet on dialysis (Hedayati et al., 2009). Fischer et al. (2012) previously reported an increase in the incidence and severity of depressive symptoms among participants from the CRIC Study, and our study supports those findings (Fischer et al., 2012). Depression screening at all stages of CKD is infrequent at best (Gyamlani et al., 2011). Our findings support the need for depression screening in mild-to-moderate CKD. It is unclear if the relationship between symptoms and depressive measures is bidirectional; therefore, longitudinal research is needed to better understand the directionality of this association.

There were differences in PCS and MCS scores at baseline between symptom subgroups. Those in the high symptom subgroup reported lower (worse) PCS and MCS scores compared to those in the moderate and low groups. Previous studies have demonstrated a negative correlation between symptom burden and PCS and MCS in ESRD patients (Almutary et al., 2013; Brown et al., 2017). Our study provides evidence that symptom subgroups are associated with PCS and MCS in individuals in mild-to-moderate CKD. Patients with CKD have reduced physical functioning and participate in less daily physical activity compared to healthy age- and gender-matched individuals (Hannan & Bronas, 2017). Our study extends these findings demonstrating a negative relationship between physical symptom subgroups and KDQOL-36 PCS scores among patients at earlier stages of CKD. Further longitudinal research is needed to understand better if symptom subgroups predict the temporal relationship between decline in PCS and MCS that occurs with progression of disease among patients with mild-to-moderate CKD. If this hypothesis is confirmed, symptom subgroups could potentially be used for risk stratification to identify

individuals for targeted patient-centered physical activity programs designed to reduce symptom burden, delay adverse effects, and improve QoL.

Race/ethnicity and gender predicted symptom cluster membership. Non-Hispanic Blacks were significantly less likely to appear in the high symptom subgroup compared to non-Hispanic Whites. Previous reports demonstrated non-Hispanic Blacks on dialysis report a higher HRQoL and experience decreased mortality compared to non-Hispanic Whites (Agodoa & Eggers, 2007; Crews, Sozio, Liu, Coresh, & Powe, 2011). This phenomenon is often referred to as the Black-White paradox and is quite controversial. Many theories have been proposed to explain this phenomenon, including differences in age (Agodoa & Eggers, 2007; Kucirka et al., 2011), BMI (Agodoa & Eggers, 2007), access to care (Norton et al., 2016), inflammatory processes (Crews et al., 2011), and lifestyle behaviors (Assari & Burgard, 2015). Additional research is needed exploring relationships of race/ethnicity and symptom clustering, as they are beyond the scope of the current study.

Women were significantly more likely to cluster into the high symptom burden group compared to men. Similar differences have been reported for patients with acute coronary syndrome (Rosenfeld et al., 2015). Sex differences in CKD have been noted previously; however, much of the literature on CKD focuses on ESRD (Carrero, Hecking, Chesnaye, & Jager, (2018). Several explanations have been offered, including biological differences related to the influence of sex hormones on symptom presentation (Carrero et al., 2018); psychological differences, including women being more open to discussing the effect of CKD on their lives compared to men (Carrero et al., 2018); and coping differences, as women are less likely to develop coping strategies that involve avoidance (Yeh & Chou, 2007). More research is needed to understand better the underlying mechanisms of higher symptom burden among women across the spectrum of CKD.

Limitations

This study is not without limitations. First, the symptom profile of the KDQOL-36 is based on a limited number of physical symptoms and may not provide a complete assessment of symptom burden, as affective symptoms are not included in the KDQOL-36. Though, the KDQOL-36 is widely used in patients with CKD, and collection of HRQoL data via the KDQOL-36 in dialysis patients is mandated by the Centers for Medicare & Medicaid Services. Nevertheless, efforts should continue to identify a comprehensive symptom instrument to assess symptom burden. Second, because we used baseline data, we were not able to determine temporal relations between baseline symptom groups and patient outcomes over time; thus, long-term change patterns of symptom subgroups and their association with changes in health outcome were not explored. Nurse scientists may use these data to advance symptom science in patients with CKD. Risk stratification using symptom subgroup data in people with mild-to-moderate stages of kidney disease may aid nurses in developing interventions at early stages of disease to delay the progression of disease and improve QoL. However, longitudinal data analysis is needed to understand better how symptom subgroup membership may change over time and the temporal associations with important clinical outcomes.

Conclusion

Using an innovative person-centered clustering approach, we identified three subgroups of patients with CKD based on the symptom profile from the KDQOL-36 and several variables that predicted membership into subgroups. Symptom subgroups could potentially be used in risk stratification, as well as inform targeted patient-centered interventions designed to reduce symptom burden, delay adverse effects, and improve QoL. Further research is needed to determine if these symptom subgroups are stable over time and can be used to predict patient clinical and healthcare utilization outcomes.

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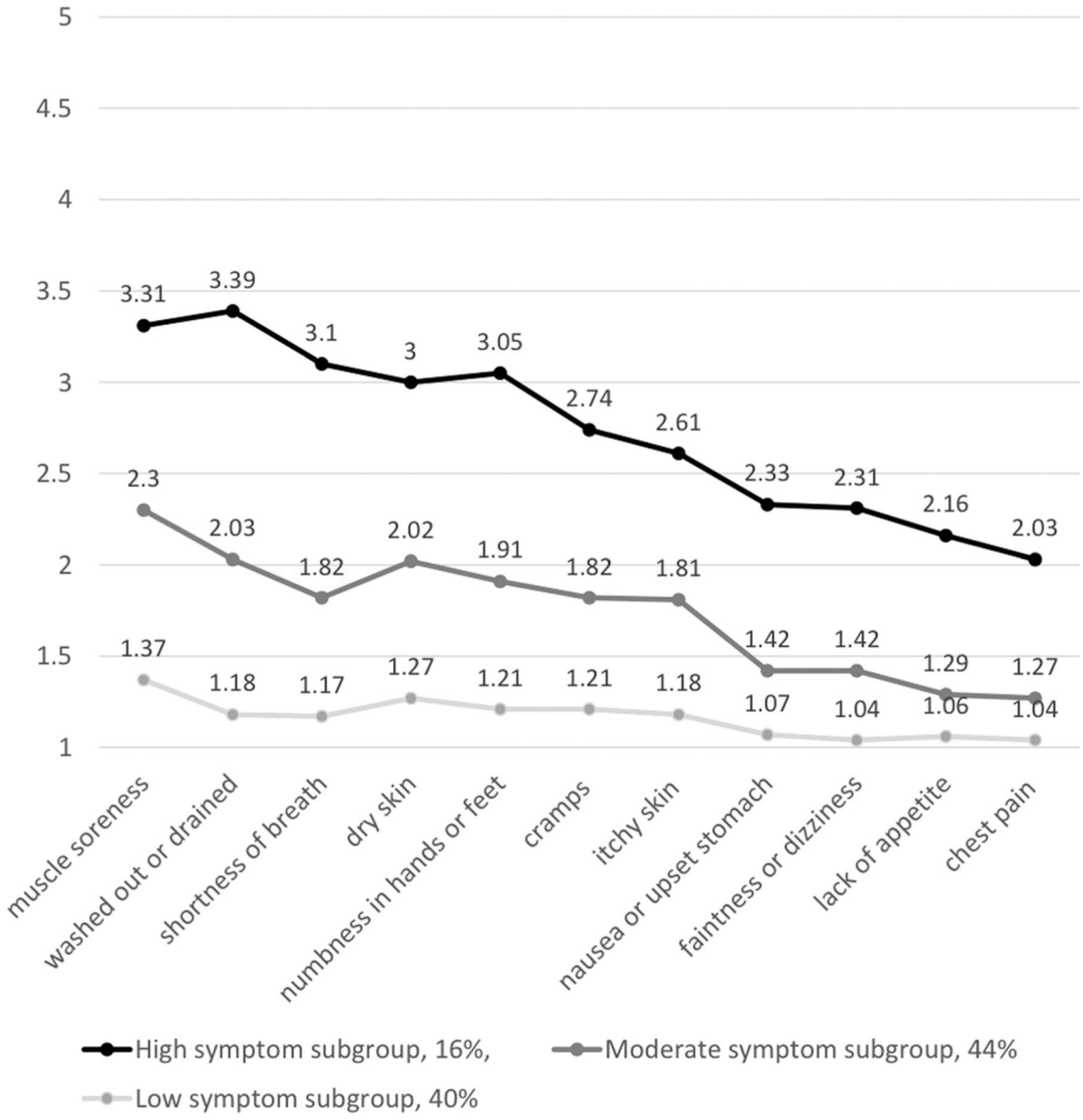

FIGURE 1.

Kidney Disease Quality of Life-36 symptom severity by symptom subgroup. Symptom cluster groups were determined using latent class analysis (LcA). Symptom features included in the LCA model were based on symptom severity (initially rated on a 5-point Likert scale: 1 = *not bothered at all*, 2 = *somewhat bothered*, 3 = *moderately bothered*, 4 = *very much bothered*, and 5 = *extremely bothered*).

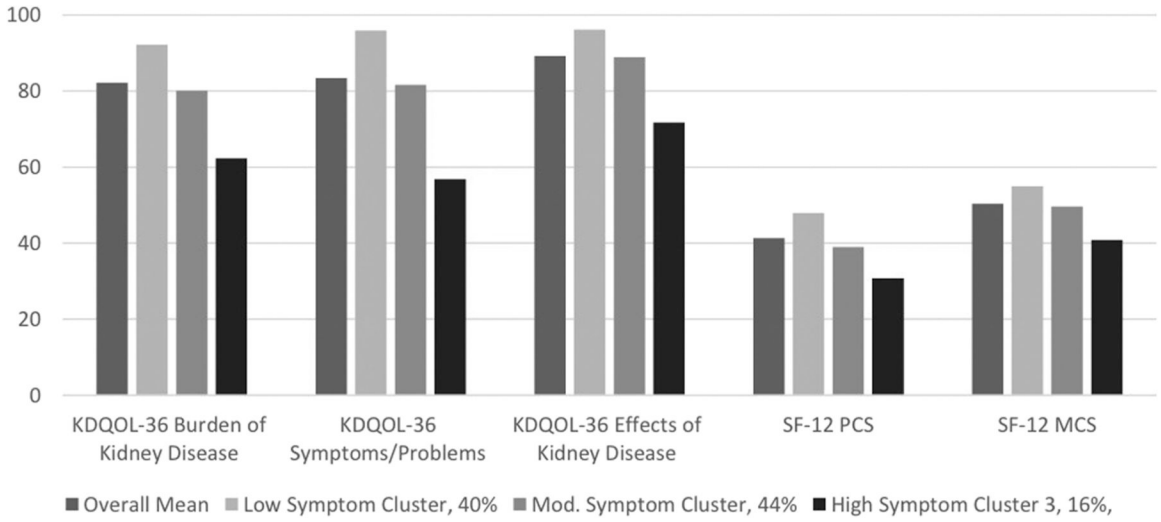

FIGURE 2.

Symptom cluster subgroups and Kidney Disease Quality of Life-36 subscale scores. Higher scores indicate better self-reported quality of life in that domain. Mod. = moderate; KDQOL = Kidney Disease Quality of Life survey; PCS = physical component summary; MCS = mental component summary.

TABLE 1.

Patient Characteristics by Symptom Subgroup (n = 3,921)

	Overall (n = 3,921)	**Low symptom group (n = 1,574)**	**Moderate symptom group (n = 1,731)**	**High symptom group (n = 616)**	
	***M* (*SD*)**	***M* (*SD*)**	***M* (*SD*)**	***M* (*SD*)**	***p***
Age (continuous)	58 (11)	58 (11)	58 (11)	57 (10)	**
eGFR (continuous)	41 (11)	43 (11)	40 (11)	39 (12)	***
BMI	32 (8)	31 (7)	32 (8)	34 (9)	***
Systolic blood pressure	129 (23)	130 (22)	129 (23)	130 (22)	**
Diastolic blood pressure	72 (13)	72 (13)	71 (13)	71 (13)	*
Beck Depression Inventory (continuous)	8.1 (7.93)	4.0 (4.7)	8.9 (7.0)	16.2 (9.8)	***
KDQOL-36 PCS	41.3 (11.52)	47.9 (8.9)	39.0 (10.7)	30.7 (9.0)	***
KDQOL-36 MCS	50.3 (10.51)	55.0 (7,4)	49.6 (10.1)	40.8 (11.3)	***
KDQOL-36 self-reported health[a]	3.3 (0.97)	2.78 (0.9)	3.41 (0.82)	4.03	***
Gender	***n* (%)**	***n* (%)**	***n* (%)**	***n* (%)**	
Female	1769 (45)	569 (58)	844 (49)	356 (58)	***
Male	2152 (55)	1005 (64)	887 (51)	260 (42)	
Race/ethnicity					
nH Black	1639 (42)	653 (42)	686 (39)	300 (49)	***
Hispanic	495 (13)	139 (9)	258 (15)	98 (16)	
nH White	1635 (42)	714 (45)	722 (42)	199 (32)	
Asian/NHP/AIAN	152 (4)	68 (4)	65 (4)	19 (3)	
Annual household income					
≤$20,000	1233 (31)	335 (21)	576 (33)	322 (53)	***
$20,001-$50,000	952 (24)	373 (24)	442 (26)	137 (22)	
$50,001-$100,000	733 (19)	381 (24)	296 (17)	56 (9)	
$100,000+	390 (10)	235 (15)	136 (8)	19 (3)	
Do not wish to answer	609 (16)	280 (16)	280 (16)	81 (13)	
Educational attainment					
High school or less	1562 (40)	529 (34)	731 (42)	302 (49)	***
Some college	1139 (29)	425 (27)	510 (30)	204 (33)	
College and beyond	110 (18)	619 (39)	490 (28)	110 (18)	

	Overall (*n* = 3,921)	Low symptom group (*n* = 1,574)	Moderate symptom group (*n* = 1,731)	High symptom group (*n* = 616)	
	M (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*p*
Marital status					
Single, separated, or divorced	1773 (45)	599 (38)	813 (47)	361 (59)	***
Married or domestic partner	2148 (55)	975 (62)	918 (53)	255 (41)	
Smoking history					
Never	1776 (45)	770 (49)	755 (44)	251 (41)	***
Former	1633 (42)	631 (40)	749 (43)	253 (41)	
Current	512 (13)	173 (11)	227 (13)	112 (18)	
Kidney disease stage					
Stage 2 (60–89 ml/min/1.73 m^2)	194 (5)	92 (6)	74 (4)	28 (5)	***
Stage 3a (45–59 ml/min/1.73 m^2)	1295 (33)	626 (40)	508 (30)	161 (26)	
Stage 3b (30–44 ml/min/1.73 m^2)	1653 (42)	628 (40)	748 (43)	277 (45)	
Stage 4 (15–29 ml/min/1.73 m^2)	779 (20)	228 (14)	401 (23)	150 (24)	
History of cardiovascular event					
Myocardial Infarction	858 (22%)	263 (17)	406 (24)	189 (31)	***
Congestive heart failure	380 (10%)	82 (5)	187 (11)	111 (18)	***
Atrial fibrillation	665 (17%)	185 (12)	326 (19)	154 (25)	***
Peripheral arterial disease	262 (7%)	49 (3)	150 (9)	63 (10)	***
Stroke	390 (10%)	121 (8)	188 (11)	81 (13)	***
Diabetes	1931 (49%)	648 (41)	914 (53)	369 (60)	***
Hypertensive	3403 (87%)	1337 (85)	1509 (87)	557 (90)	***

Note. eGFR = estimated glomerular filtration rate; BMI = body mass index; KDQOL = Kidney Disease Quality of Life; PCS = physical composite score; MCS = mental composite score; nH = non-Hispanic; NHP = Native Hawaiian Pacific Islander; AIAN = American Indian Alaska Native.

[a]KDQOL-36 self-reported health was rated on a Likert-type scale (1 = *excellent*, 2 = *very good*, 3 = *good*, 4 = *fair*, 5 = *poor*). Higher scores indicate worse health.

*$p < .05$.

**$p < .01$.

***$p < .001$.

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TABLE 2.

Model Fit by Different Number of Classes

Likelihood		BIC	AIC	SSBIC	LMR LR test	VLMR LR test	Bootstrap LR Test	Entropy
1	−47467.668	95390.663	95045.336	95215.898				
2	−43833.858	88586.649	87889.715	88233.941	<.001	<.001	<.001	0.821
3	−42935.032	87252.605	86204.065	86721.954	<0.0001	<0.0001	<.0001	0.884
4	−42199.038	86244.222	84844.076	85535.629	<0.0001	<0.0001	<0.0001	0.813
5	−41904.745	86119.242	84367.49	85232.707	0.7604	0.7604	<.0001	0.762
6	−41646.907	86067.173	83963.815	85002.695	0.6229	0.6232	<.0001	0.750
7	−41460.344	86157.653	83702.689	84915.233	0.7604	0.7604	<.0001	0.757

Note. Entropy at an omnibus index of >0.8 indicates good classification. BIC = Bayesian information criterion; AIC = Alkaike information criterion; SSBIC = sample size adjusted BIC; LMR LR = Lo-Mendell-Rubin likelihood ratio test; VLMR LR = Vuong-Lo-Mendell-Rubin likelihood ratio test; LR = likelihood ratio.

TABLE 3.

Multinomial Logistic Regression for Membership Into High Symptom Subgroup Compared to Low Symptom Subgroup (n = 3,791)

Variables	Overall (n = 3,791) RRR (95% CI)
Age (continuous)	0.97 (0.96–0.99)***
Race/ethnicity (referent nH White)	
nH Black	0.63 (0.46–0.87)**
Hispanic/Latino	0.76 (0.48–1.21)
Asian/NHP/AIAN	0.95 (0.45–2.00)
Gender (referent female)	0.62 (0.46–0.82)***
Marital status (referent married/domestic partner)	
Single/separated/divorced	1.23 (0.92–1.64)
Household income (over $100,000)	
$50,0001–$100,000	0.88 (0.44–1.76)
$20,001-$50,000	1.24 (0.63–2.44)
≤$20,000	1.48 (0.73–3.00)
Do not wish to answer	1.10 (0.54–2.26)
Education attainment (referent college and beyond)	
Some college	1.28 (0.87–1.88)
High school or less	0.85 (0.57–1.27)
Smoking habit (referent never)	
Former	1.17 (0.87–1.57)
Current	0.96 (0.64–1.46)
eGFR (continuous)	0.98 (0.97–0.99)***
Diabetes	0.99 (0.73–1.32)
BMI (continuous)	0.99 (0.98–1.01)
Systolic blood pressure (continuous	1.00 (0.99–1.01)
Diastolic blood pressure (continuous)	1.00 (0.99–1.01)
History of cardiovascular event (referent no history)	
Myocardial infarction	1.29 (0.93–1.81)
Congestive heart failure	1.67 (1.07–2.61)*
Atrial fibrillation	1.65 (1.17–2.34)**
Peripheral arterial disease	1.79 (1.07–3.02)*
Stroke	0.65 (0.43–0.99)*
KDQOL-36 PCS (continuous)	0.85 (0.83–0.90)***
KDQOL-36 MCS (continuous)	0.88 (0.87–0.90)***
Beck Depression Inventory (continuous)	1.13 (1.10–1.15)***

Note: nH = non-Hispanic; NHP = Native Hawaiian Pacific Islander; AIAN = American Indian Alaska Native; eGFR = estimated glomerular filtration rate; BMI = body mass index; KDQOL = Kidney Disease Quality of Life; PCS = physical composite score; MCS = mental composite score; RRR = relative risk ratio.

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*$p < .05$.

**$p < .01$.

***$p < .001$.