Original Article

Symptom Clusters From Dialysis to Renal Transplantation: A Five-Year Longitudinal Study

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Abstract

Context. Patients on dialysis experience multiple concurrent and often related symptoms defined as symptom clusters. Renal transplantation (RTX) is thought to reduce symptom experience and improve health-related quality of life. No longitudinal study has assessed symptoms and symptom clusters in patients in the transition from dialysis to RTX.

Objectives. We aimed to assess changes in symptom prevalence, identify symptom clusters after RTX, and evaluate the effect of the treatment conversion on predefined symptom clusters.

Methods. A cohort of patients on chronic dialysis ($n = 110$) was followed prospectively with measurements of health-related quality of life using the Kidney Disease and Quality of Life-Short Form (KDQOL-SF) during dialysis (baseline) and after subsequent RTX. Predefined symptom clusters based on 11 symptoms listed in KDQOL-SF were previously generated using principal component analysis with varimax rotation, that is, uremic (nausea, lack of appetite, dizziness, feeling squeezed out, shortness of breath, and chest pain), neuromuscular (numbness, sore muscle, and cramps), and skin (itching and dry skin) clusters. Stratified analyses were undertaken to identify characteristics associated with change in the symptom clusters after RTX. Cohen's d was used as effect size.

Results. Of the 110 patients, mean age was 51.3 ± 14.4 years, and 66% were males. After RTX, the estimated glomerular filtration rate was 54 (interquartile range [IQR] 45–72) mL/minute/1.73 m^2. Median follow-up time from assessments during dialysis was 55 (IQR 50–59) months, and follow-up time after RTX was 41 (IQR 34–51) months. The total symptom score improved (73 ± 16 vs. 82 ± 15, $P = 0.001$, and Cohen's $d = 0.6$), and the number of symptoms was reduced (6.5 ± 2.6 vs. 4.7 ± 3.0, $P = 0.001$). Seven symptoms improved statistically after RTX, but only two with Cohen's $d > 0.5$ (itching and cramps). The scores of the predefined symptom clusters improved after RTX: uremic (82 ± 16 vs. 85 ± 17, $P = 0.008$, and Cohen's $d = 0.2$), neuromuscular (66 ± 24 vs. 79 ± 18, $P = 0.001$, and Cohen's $d = 0.6$), and skin cluster (62 ± 27 vs. 78 ± 22, $P = 0.001$, and Cohen's $d = 0.6$). Symptom clusters could not be generated after RTX.

Conclusion. Although symptoms and symptom clusters were reduced after RTX, the clinical relevance of the reductions was ambiguous. Symptom clusters could not be generated after RTX, suggesting that use of the KDQOL-SF may not be optimal to assess symptoms in RTX patients. J Pain Symptom Manage 2016;51:512–519.

Key Words

Symptoms, symptom clusters, longitudinal study, renal transplantation

Introduction

The symptom burden in dialysis patients is substantial[1–3] and associated with reduced health-related quality of life (HRQOL).[1,4,5] Symptoms in dialysis patients may be related to the loss of renal function and associated treatments, as well as comorbid medical conditions.[3,6,7] Symptoms rarely occur in isolation. Most patients experience multiple co-

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occurring symptoms.[1,6,8,9] Initially, the concept of a symptom cluster was described in cancer patients.[10,11] Recently, our research team[1,12] and others[6,8,9] have evaluated symptom clusters in renal patients. A symptom cluster is defined as two or more co-occurring symptoms that are related to each other and may share the same etiology.[13,14] Based on the physical symptoms listed in the Kidney Disease Quality of Life-Short Form (KDQOL-SF) questionnaire,[15] we have previously identified three distinct symptom clusters in dialysis patients.[1] These symptom clusters were closely associated with decrements in HRQOL and predicted mortality.[12]

Renal transplantation (RTX) is the optimal treatment option for patients with end-stage renal disease. Previous cross-sectional studies have revealed improvements in HRQOL after RTX.[16–18] Relief of some symptoms is expected after RTX because uremic and dialysis-related symptoms are alleviated. However, RTX patients may continue to experience symptoms related to graft dysfunction, as well as symptoms associated with medications and other comorbid conditions.[19–21]

Most data on symptoms in RTX patients are based on cross-sectional studies.[19–22] Only one study was identified that described symptom clusters after RTX.[19] To our knowledge, no study has evaluated symptom clusters in patients during the transition from dialysis to RTX. An assessment on predefined symptom clusters from dialysis to RTX would provide the patients' unique perspective on the impact of treatment. We postulate that the scores in the predefined symptom clusters observed during dialysis would improve after RTX.

Therefore, the purposes of this longitudinal cohort study were to assess change in symptom prevalence in a cohort of patients with end-stage renal disease during dialysis and after RTX, to evaluate the effect of this treatment conversion on predefined symptom clusters, and to explore the symptom clusters after RTX.

Methods

Patients and Study Design

From an initial cohort of 301 patients who were included in a cross-sectional study between August 2005 and February 2007, 159 patients were alive and had received RTX or were on dialysis. These patients were invited to participate in the present follow-up study in years 2010 and 2011 (Fig. 1). Patients were recruited from 10 different hospital-based dialysis units across Norway. As described previously,[23] patients older than 18 years receiving either hemodialysis or peritoneal dialysis for more than two months and who were in a clinically stable condition were eligible to participate. Adequate Norwegian language skills and signed informed consent were prerequisites for enrollment. Patients with cognitive dysfunction, psychosis, or drug abuse were excluded. Although hospitalization led to exclusion, patients could be included four weeks after being discharged from the hospital if they were in a clinically stable condition. Study nurses and physicians were trained to administer the study instruments. The same exclusion criteria were applied in the follow-up study. The study was approved by the Regional Committees for Medical and Health Research Ethics in Norway, and concession to store data was obtained from the National Data Inspectorate.

Demographic and clinical data were obtained through self-administered questionnaires and the patients' medical records. Data with regard to transplantation were retrieved from the Norwegian Renal Registry.[24] The Charlson Comorbidity Index (CCI), which has been validated for both dialysis[25] and RTX patients,[26] was used to measure comorbidity. The CCI provides a composite score for 17 comorbid conditions (e.g., coronary artery disease, congestive heart failure, diabetes, chronic renal failure, diabetic organ damage) and age. Scores can range from one to six for each comorbid condition, and a score of one is added for each decade after 40 years. In this study, age was not included in the calculation of CCI because age was entered as a separate variable in the statistical analyses.

The KDQOL-SF is a valid, reliable, and widely used questionnaire developed by the Research and Development Group to measure generic and disease-specific HRQOL in patients with kidney disease.[15,27,28] The generic part of the questionnaire is equivalent to the SF-36 questionnaire, which consists of 36 items.

Symptoms is one of 11 scales in the kidney-specific part of the KDQOL-SF, version 1.3. Symptoms consist of 12 separate items. In the present study, dialysis access was omitted as this information was not relevant in RTX patients. The 11 remaining symptoms were muscle soreness, chest pain, cramps, itching, dry skin, shortness of breath, feeling dizzy, lack of appetite, feeling squeezed out, numbness in the extremities, and nausea. Patients were asked to rate how bothered they were by these symptoms over the last four weeks using a five-point Likert scale (i.e., 1 = not bothered at all, 2 = somewhat, 3 = moderately, 4 = very much, and 5 = extremely bothered). Each symptom was given a score based on the Likert scale that ranged from 0 (extremely bothered, the worst perceived state) to 100 (not bothered at all, the best perceived state). Patients with symptom scores 0 and 25 were categorized as very much to extremely bothered, 50 and 75 somewhat to