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ORIGINAL ARTICLE

Differences in Quality of Life Outcomes Among Depressed Spinal Cord Injury Trial Participants

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Abstract

Objective: To assess the role that treatment response plays in a randomized controlled trial of an antidepressant among people with spinal cord injury (SCI) diagnosed with major depressive disorder (MDD) in explaining quality of life (QOL), assessed both globally as life satisfaction and in terms of physical and mental health-related QOL.

Design: Multivariable analyses were conducted, controlling for demographic, neurologic, and participatory factors and perceived functional limitations.

Setting: Rehabilitation centers.

Participants: Of the 133 persons who were randomized into the Project to Improve Symptoms and Mood after Spinal Cord Injury randomized controlled trial, 124 participated in this study. All participants were between the ages of 18 and 64 years, at least 1 month post-SCI, met the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition*, criteria for MDD, and completed the core measures used in this study.

Interventions: Not applicable.

Main Outcome Measures: The Satisfaction with Life Scale and the physical and mental component summary scores of the Medical Outcomes Study 12-Item Short-Form Health Survey.

Results: Reduction in depressive symptoms over the course of a 12-week trial was predictive of increased QOL, which was measured as life satisfaction and mental well-being, within the context of other explanatory factors. However, reduction in symptoms did not explain differences in physical well-being among those with MDD. Perceived functional disability explained all 3 indices of QOL.

Conclusions: Greater recognition has been given to QOL outcomes as endpoints of clinical trials because these often reflect participants' reported outcomes. Our findings support the association of QOL to the reduction of depression symptoms among trial participants. This association differs depending on how QOL is defined and measured, with stronger relations observed with life satisfaction and mental well-being among those diagnosed with MDD. The lack of association between depression and physical well-being may be explained by participants' subjective interpretation of physical well-being after SCI and their expectations and perceptions of improved physical health-related QOL based on the use of assistive technology. Consistent with our findings, pain is likely to play a role in decreasing physical QOL among those with incomplete injuries. Practicing caution is suggested in using physical well-being as an endpoint in trials among people with SCI.

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Depression is a treatable risk factor for poor quality of life (QOL).[1,2] In persons with spinal cord injury (SCI), depression is associated with numerous physical and emotional symptoms. Although its prevalence varies depending on the characteristics of the sample and methods of assessment, several authors have reported estimates in the range of 15% to 35%.[3-6] Worsening health

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problems, presence of pressure ulcers, pain, and lack of effective treatment can exacerbate symptoms, contributing to high rates of chronic and recurrent depression[4,7] and reduced QOL.[8]

One problem that has limited the utility of some QOL research is that it is used to mean a variety of different things, including health status, physical functioning, psychosocial adjustment, life satisfaction, and happiness.[9] For the purposes of this study, we are defining QOL as both life satisfaction and health-related quality of life (HRQOL), which has 2 principal components, physical and mental.[10] This study focused on participants with SCI who were diagnosed with major depressive disorder (MDD) using the Structural Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition* (SCI-DSM-IV).[11] Study diagnostic criteria included having at least 5 of 9 symptoms (eg, depressed mood, a loss of interest or pleasure in daily activities) for >2 weeks.[12]

Measurement of QOL is becoming increasingly recognized as an important endpoint in clinical trials.[13] Although reducing depression symptoms is the primary goal in depression trials, depression studies with non-SCI populations have focused on QOL as a secondary outcome.[14,15] Rapaport et al[16] examined QOL outcomes from 11 treatment trials for depression in non-SCI samples and found that 63% of patients with MDD had severe QOL impairments. Similarly, MDD is associated with poor QOL among patients with psychiatric disorders.[17] IsHak et al[18] found that severity of depression is a major contributor to reduced QOL, whereas Gaynes et al[19] found a similar relation between depression and HRQOL in a sample of 9898 persons aged 25 to 74 years and living in the community.

Despite its importance, much less attention has been given to using QOL as an outcome of rehabilitation interventions.[20]

Although there are a number of correlational studies that support a relation between depression, HRQOL, and life satisfaction after SCI,[21-23] it is unclear if reduction in depression is associated with improvement in QOL. Contributors to QOL after SCI are varied and include lifestyle characteristics, environmental factors, health status, and relations.[24,25] Similarly, community participation and physical activity may influence HRQOL and life satisfaction.[26,27]

List of abbreviations:

AIS	**ASIA (American Spinal Injury Association) Impairment Scale**
CHART-SF	**Craig Handicap Assessment and Reporting Technique Short Form**
HAMD	**Hamilton Depression**
HRQOL	**health-related quality of life**
MCS	**mental component summary**
MDD	**major depressive disorder**
PCS	**physical component summary**
PRISMS	**Project to Improve Symptoms and Mood after Spinal Cord Injury**
QOL	**quality of life**
SCI	**spinal cord injury**
SCI-DSM-IV	**Structural Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition***
SDS	**Sheehan Disability Scale**
SF-12	**Medical Outcomes Study 12-Item Short-Form Health Survey**
SWLS	**Satisfaction with Life Scale**
VIF	**variance inflation factor**

The use of QOL outcomes in clinical trials poses several challenges. Research is complicated by the multidimensional nature of QOL and its relations to many aspects of life. A number of factors may moderate its relation with depression.[28] In persons with SCI, psychological adjustment may be impeded by lack of access to resources, which in turn reduces ability to fully participate in society.[29] The methods used to assess QOL, as multidimensional or global constructs, may also influence study outcomes. Furthermore, most of the measures used to assess QOL were developed for able-bodied persons, without assessment of their psychometric properties in the SCI population.[24] Therefore, the validity of some measures may be questionable.

This study reports on secondary analyses of QOL outcomes in a community-based sample of persons with SCI who participated in a randomized controlled trial of venlafaxine XR to treat MDD. The trial is entitled the Project to Improve Symptoms and Mood after Spinal Cord Injury (PRISMS). The result of the PRISMS study indicated that participants treated with venlafaxine XR had greater improvements in depression symptoms as measured by the Maier subscale of the Hamilton Depression (HAMD) scale than placebo controls. Treatment with venlafaxine XR, however, was not associated with greater improvement in QOL.[30]

This article addresses differences in QOL outcomes as a function of reduction in depressive symptoms from study baseline to the end of the intervention. Reduction in depressive symptoms was defined both as the reduction in scores on the study's measure of depression and as trial response status. Trial responders are defined as those with clinically significant reductions in depressive symptoms regardless of treatment group assignment; nonresponders are defined as those without such reductions. The study examines whether reduction in depressive symptoms influences QOL in the context of participants' demographic and injury characteristics, perceived functional disability, and selected indices of participation. We were interested in assessing if these associations differ when QOL is measured multidimensionally as HRQOL or globally as overall life satisfaction. Findings help clarify whether improvement in QOL can be expected from effective treatment of MDD and guide the use of QOL outcomes in future SCI-related clinical trials.

We hypothesized that reductions in depression symptoms among participants with SCI would be associated with superior QOL outcomes, regardless of whether QOL was assessed as HRQOL or as global life satisfaction. We expected that this relation would be observed in terms of physical HRQOL, mental HRQOL, and global life satisfaction.

Methods

Data were from the 6 sites participating in the PRISMS multicenter double-blind placebo controlled trial. Potential participants were approached either because they were participants in the SCI Model Systems, in which 4 of the sites were participating, or because they responded to a study advertisement indicating potential interest. Participants were recruited from outpatient clinics and inpatient rehabilitation units through posted flyers and referrals. The study also recruited via newsletters, webpage advertisements, and e-mail listservs. Potential participants were approached in person by study staff or by telephone and screened for MDD using the Patient Health Questionnaire (9-item screen for depression) and the SCI-DSM-IV.[12]

The PRISMS study investigated the efficacy and tolerability of venlafaxine XR for treatment of MDD. The intervention consisted