Quality of Life and Self-Reported Lower Extremity Function in Adults with HIV-related Distal Sensory Polyneuropathy

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Greetings from NEW JERSEY
BACKGROUND

- Distal Sensory Polyneuropathy is the most common neurological comorbidity in patients with HIV disease 1-2

- Studies of patients with HIV disease have reported neuropathy prevalence ranging from 38% to 53% 1, 3-5

- Individuals with HIV-related DSP typically experience pain, numbness, paresthesia, reduced quality of life compromised function, and episodic disability 6-7

- Neuropathic pain has been associated with disability in ADLs, unemployment, and compromised quality of life (QOL) 1

- Antiretroviral therapy may increase intensity and frequency of neuropathic symptoms 5
BACKGROUND

Pathophysiology of DSP is not fully understood, but has been related to:
- Peripheral nerve damage related to HIV infection \(^8-^9\)
- Toxic effects of certain anti-retroviral drugs \(^1\)

Risk factors for DSP in people with HIV disease include \(^1, ^{10-14}\)
- Advancing age
- Past exposure to certain anti-retroviral drugs
- Longer duration (history) of HIV infection
- Advanced HIV disease
- Substance abuse
- Low CD4 nadir

The impact of DSP on QOL and function in individuals with HIV disease needs to be elucidated.
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Purposes

- Compare QOL and self-reported lower limb function in HIV+ patients with and without DSP
- Determine the degree to which self-reported lower limb function predicts QOL
- Evaluate agreement (concordant validity) between the Lower Extremity Function Scale (LEFS) and the Lower Limb Functional Index (LLFI) in this population
- Describe utilization of health care resources for pain management in HIV+ patients with and without DSP
Methods

• Participants were patients at an infectious disease practice in southern New Jersey
  • sample of convenience
  • 94 signed informed consent
    • 82 had usable MOS-HIV data
    • 3 with concurrent diagnosis of diabetes
  • data obtained from approximately 8% of HIV+ caseload at GSIDA

• Inclusion criteria
  • history of HIV disease
  • ambulatory
  • ability to read and write in English

• Exclusion criteria
  • active opportunistic infections
  • uncontrolled psychiatric disorders
Methods

• Data collection
  • Demographic questionnaire and chart review
  • **MOS-HIV** (Physical Summary Score and Mental Summary Score)
  • **Lower Extremity Functional Scale (LEFS)**
  • **Lower Limb Functional Index (LLFI)**
The Lower Extremity Functional Scale

We are interested in knowing whether you are having any difficulty at all with the activities listed below because of your lower limb problem for which you are currently seeking attention. Please provide an answer for each activity.

Today, do you or would you have any difficulty at all with:

<table>
<thead>
<tr>
<th>Activities</th>
<th>Extreme Difficulty or Unable to Perform Activity</th>
<th>Quite a Bit of Difficulty</th>
<th>Moderate Difficulty</th>
<th>A Little Bit of Difficulty</th>
<th>No Difficulty</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Any of your usual work, housework, or school activities.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2 Your usual hobbies, recreational or sporting activities.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3 Getting into or out of the bath.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4 Walking between rooms.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5 Putting on your shoes or socks.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6 Squatting.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7 Lifting an object, like a bag of groceries from the floor.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8 Performing light activities around your home.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9 Performing heavy activities around your home.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10 Getting into or out of a car.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>11 Walking 2 blocks.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>12 Walking a mile.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>13 Going up or down 10 stairs (about 1 flight of stairs).</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>14 Standing for 1 hour.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>15 Sitting for 1 hour.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>16 Running on even ground.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>17 Running on uneven ground.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>18 Making sharp turns while running fast.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>19 Hopping.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>20 Rolling over in bed.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

**Column Totals:**

Minimum Level of Detectable Change (90% Confidence): 9 points  
SCORE: ____ / 80

Demographic and Clinical Characteristics of the sample

- **Gender**
  - 55 men (54.5% had DSP)
  - 29 women (43.6% had DSP)

- **Race**
  - 40 Caucasian (47.3% had DSP)
  - 41 African American (50.9% had DSP)
  - 1 other (had DSP)

- **Age**
  - Mean: 42.1 years (those without DSP)
  - Mean: 49.5 years (those with DSP)

- **Years with HIV**
  - Mean: 11.8 years (those without DSP)
  - Mean: 15.4 years (those with DSP)

- **CD4 counts (cells/mm³)**
  - Mean: 526 (those without DSP)
  - Mean: 534 (those with DSP)

- **Viral load (copies/mL)**
  - n=40 undetectable
  - n=32 low (20-100,000)
  - n=5 high (>100,000)
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<table>
<thead>
<tr>
<th>Measure</th>
<th>Participants Without Foot DSP</th>
<th>Participants With Foot DSP</th>
<th>$p^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$n$</td>
<td>$\bar{X}$ (Range)</td>
<td>SD</td>
</tr>
<tr>
<td>LLFI</td>
<td>28</td>
<td>76.2 (30–100)</td>
<td>27.1</td>
</tr>
<tr>
<td>LEFS (raw score)</td>
<td>27</td>
<td>62.2 (14–80)</td>
<td>22.4</td>
</tr>
</tbody>
</table>

*a LLFI=Lower Limb Functional Index, LEFS=Lower Extremity Functional Scale, DSP=distal sensory polyneuropathy.

*b Determined with the Mann-Whitney test; significance tests were within tools.

*c $n=80$; data for 2 participants were missing.
Bottom Lines
Self-reported LE function, using either the LEFS or the LLFI, was significantly lower in HIV+ patients with DSP than in those without DSP. Scores reflect ≤50% of normal/full function in those with DSP.

Mean LLFI score 32.8 points lower in those with DSP
Mean LEFS score (raw) 21.2 points lower in those with DSP
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### Physical and Mental Health Summary Scores by Foot DSP Diagnosis (n=74)

<table>
<thead>
<tr>
<th>Summary Score</th>
<th>Participants Without Foot DSP</th>
<th>Participants With Foot DSP</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>X</td>
<td>SD</td>
</tr>
<tr>
<td>Physical health</td>
<td>24</td>
<td>47.9</td>
<td>23.2</td>
</tr>
<tr>
<td>Mental health</td>
<td>24</td>
<td>47.8</td>
<td>28.0</td>
</tr>
</tbody>
</table>

For 8 of the 82 participants for whom Medical Outcomes Study HIV Health Survey data were complete, the data for years with HIV disease or years receiving disability were missing; therefore, data from 74 participants were included in the analysis. DSP = distal sensory polyneuropathy.

Determinated with general linear models adjusted for sex, age, years with HIV disease, HIV disability, and interactions; significance tests were within summary scores.

Normalized.
Bottom Line
Physical Summary Score component of quality of life (MOS-HIV) significantly lower in HIV+ participants with DSP than those without.

Mean Physical Summary Score 15.2 points lower in those with DSP
• Relationship between QOL, potential confounders, and LE function

• Regression models of the effects of LLFI and LEFS predicting physical and mental quality of life were statistically adjusted by including potential confounders (employment status, disability benefit status, presence of foot DSP, age, and PT treatment); this resulted in parameter estimates of the relationships of LEFS and LLFI and the quality of life variables after controlling for the effects of the covariates.

• BOTTOM LINE: Lower limb function scores were highly predictive of both physical and mental QOL after controlling for confounders.

  • The models predicted between 68% and 75% of the variance in physical quality of life and approximately 31% of the variance in mental quality of life (physical quality of life: R²=.675 for LLFI and R²=.749 for LEFS; mental quality of life: R²=.310 for LLFI and R²=.309 for LEFS (p<0.001 for all models)

  • Of potential confounders entered into the models, only employment status was associated with physical summary score aspect of QOL (after controlling for LLFI and LEFS scores).
Bland-Altman analysis to assess agreement between scaled LEFS and LLFI: (+) score indicates scaled LEFS overestimates LLFI (i.e., LLFI indicates that the patient has a lower level of functioning than LEFS), and a (-) score indicates that scaled LEFS underestimates (i.e., patient has lower function) than LLFI.

Band of clinically relevant agreement: 11.25 points (MCID of the LEFS)

Mean difference in LEFS and LLFI was 6.2 (significantly different than zero) indicating that, on average, the scaled LEFS overestimates LLFI by about 6 points.

LEFS approximates LLFI within the band of clinical agreement in 58.8% (n=47) of the subjects, underestimating LLFI (indicating worse function) in only 10% of the cases (n=8), while overestimating LLFI in 31.3% (n=25) of the subjects. LLFI is likely to classify patients as having a level of physical functioning equal to or lower than LEFS in 90% of subjects. LLFI is more likely to identify patients as having lower self-reported function than the LEFS.

A similar pattern was found when LEFS and LLFI were further analyzed by subgrouping for patients with and without DSP. The LLFI was even more likely to indicate impairments in lower extremity function in those with DSP than the LEFS.
Analysis of the magnitude of disagreement between LEFS and LLFI revealed a wider degree of disagreement among patients with DSP than in patients without DSP with an interquartile range (IQR) among patients with DSP (IQR=19.3) approximately 3.7 times greater than the IQR for patients without DSP (IQR=5.3).

This indicates that not only can the clinician expect LEFS to overestimate LLFI, but the degree of the overestimate is likely to be even less predictable in patients with DSP than in patients without DSP.

**Bottom Lines**

Findings suggest **concordant validity** of the LEFS and LLFI in patients with HIV disease.

Our findings suggest that the **LLFI may be preferable to the LEFS** to identify activity limitations (functional impairments) **in patients with HIV-related DSP**.
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Bottom Line
Significant higher rates of utilization of pain management (medical or PT or CAM) in HIV+ participants with DSP
Limitations

• Sample of convenience may explain our higher than expected DSP prevalence rate of 67%

• Single location in northeast US

• Diagnosis of DSP based on self-report (Single Question Neuropathy Scale) with confirmation from medical chart when possible
  • SQNS specificity for DSP = 80%, possibly inflated our prevalence estimate

• Due to our small size, post hoc analysis revealed we were underpowered to detect a difference in Mental Health Summary Scores

• Reliance on self-report of function / activity limitation

• Although we did not explore reasons for compromised function and QOL in those without DSP; likely related to other comorbidities and/or side effects of HAART
Quantitative Measures of LE Function\textsuperscript{15,16}

2011 \textit{High Frequency of Poor Locomotor Performance in HIV+ Patients}
- BERG Balance Scale, 6 MWD, TUG, Functional Reach Test, One-leg Stance Test, 5X sit-to-stand
- 1 of 2 adults had poor LE muscle performance which may put this group at risk for falls and fractures

2014 \textit{Decline in Locomotor Functions Over Time in HIV+ Patients}
- Compared to healthy persons baseline 5X STS and 6MWD were poorer in HIV+ adults and associated falls.
- Test performances deteriorated further over time
- Age, diabetes, neurologic complications, injection drug use, rather than virologic factors contribute to variations in LE muscle performance
Future study is needed to:

• Further determine validity and reliability of LEFS and LLFI in this population

• Combine patient reported outcome measures and objectively quantify LE performance (including gait) to further describe effects of HIV-related DSP on function

• Explore effectiveness of non-pharmacologic interventions for HIV-related DSP on key outcomes such as pain, QOL, function, balance, gait, and peripheral nerve function
  • Physical therapy
    • Electrical Modalities
    • Manual therapy
    • Exercise
  • Movement based activities
    • Yoga
    • Tai Chi
References


