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Quantitative Evaluation of an Instrument to Identify Chronic Pain in HIV-Infected Individuals

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Abstract

A method to rapidly identify the presence of chronic pain would enhance the care of HIV-infected individuals, but such an instrument has not been assessed in this population to date. We assessed the construct validity of the two-question Brief Chronic Pain Questionnaire (BCPQ) in HIV-infected patients by assessing the association between BCPQ responses and known correlates of chronic pain. Participants in the University of Alabama Center for AIDS Research Network of Integrated Clinical Systems cohort completed the BCPQ, along with the EuroQOL to assess physical function, the PHQ-9 to assess depression, and the PHQ-anxiety module to assess anxiety. Among 100 participants, 25% were female, the mean age was 45 (SD 12), 63% were African American, 27% were publicly insured, the median $CD4^+$ T cell count was 572 cells/mm^3 (IQR 307–788), and 82% had an undetectable viral load. Participants with chronic pain were more likely to have impaired mobility (43% vs. 12%, $p = 0.001$), difficulty with usual activities (47% vs. 12%, $p < 0.001$), lower overall health state (70 vs. 84, $p = 0.002$), pain today (80% vs. 27%, $p < 0.001$), depression (30% vs. 15%, $p = 0.10$), and anxiety (43% vs. 10%, $p < 0.001$) than those without chronic pain. This study provides preliminary evidence for the BCPQ as a brief questionnaire to identify the presence of chronic pain in HIV care settings.

Introduction

Chronic pain—persistent pain beyond the period of normal tissue healing—is a common chronic condition.[1] It is heterogeneous, and includes conditions such as peripheral neuropathy, local and widespread musculoskeletal pain, and headache.[2]

Chronic pain is an important comorbidity in HIV-infected individuals. Precise prevalence estimates are lacking, as there is no widely used, well-studied tool to identify the presence of chronic pain in the general population, or in HIV-infected patients. Recent studies of HIV-infected patients use various instruments to estimate the prevalence of chronic pain, from asking about pain ''today'' to asking about pain repeatedly over time. These studies suggest that the prevalence of chronic pain in HIV-infected patients may be anywhere from 30% to as high as 85%.[3] In HIV-infected patients, pain is highly clinically significant—it is associated with up to 10 times greater odds of functional impairment,[4] and in some patients, suboptimal retention in HIV primary care.[3]

A brief questionnaire to identify chronic pain in HIV-infected individuals would enhance both patient care and research in this population, as it would efficiently identify individuals with chronic pain who benefit from pain-focused assessment and treatment, and enrollment in relevant studies. Formal screening tools are most easily developed in situations in which a gold standard exists.[5] For chronic pain, no such gold standard, such as a standardized interview, exists. Although biomarkers for pain are in development,[6–8] they are not ready for diagnostic use.

Pain's inherently subjective nature confers particular importance to self-report; if patients say they have pain, they have pain. Operational definitions of chronic pain include a timeframe of > 3–6 months, and pain that persists beyond the

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period of tissue injury.[9,10] To be useful to clinicians, a brief questionnaire to identify chronic pain should at minimum query (1) self-report of pain and (2) chronicity.

The recently developed Brief Chronic Pain Questionnaire (BCPQ)[11] combines one item from the well-studied SF-8[12] (''How much bodily pain have you had during the last week?'': none, very mild, mild, moderate, severe, very severe), with a chronicity question (''Do you have bodily pain that has lasted for more than three months?'': no, yes). It has been assessed among healthy Norwegians,[11] but not in any clinical population, including patients with HIV. Previously, we performed initial qualitative testing of the BCPQ in HIV-infected patients, and found that it is well-understood and straightforward.[13] The objective of the current study was to quantitatively investigate the BCPQ through an initial test of construct validity, by assessing the association between the BCPQ and other known clinical correlates of chronic pain.

Materials and Methods

This study was conducted at the University of Alabama at Birmingham's HIV clinic, which cares for 2,000 HIV-infected patients, most of whom are enrolled in the Center for AIDS Research Network of Integrated Clinical Systems (CNICS). CNICS captures demographic and clinical data; additionally, participants complete numerous well-validated electronic Patient Reported Outcome (PRO) measures on a variety of topics every 6 months.[14,15] We recruited 100 CNICS participants to complete a paper-and-pencil version of the BCPQ.

Using the BCPQ, chronic pain was defined as pain of at least mild severity for at least 3 months. We applied a cutoff of mild severity for several reasons. Although many studies dichotomize patients having pain of mild severity (e.g., <4 on a 0–10 scale) versus moderate or greater severity (≥ 4), there is no compelling evidence that this distinction is clinically relevant. In fact, there is some evidence that this classification misses some clinically important pain.[16] For a brief instrument, in which subsequent assessment (i.e., administration of the Brief Pain Inventory) would be low risk, we opted to err on the side of inclusiveness.[17–19]

The validity of a tool is its ability to measure what it is intended to measure. The validity of the BCPQ is its ability to measure chronic pain. Assessing a tool's validity is a process that, in its entirety, can take years, or even decades, of testing the tool's performance. For example, the SF-36, a tool that has been in wide use for decades, continues to undergo validation of its use in various settings and for various purposes.[20–23]

Tests of construct validity assess whether an instrument or questionnaire performs the way we would expect, based on what we know or would hypothesize about the phenomenon being measured.[5,24] Persons with chronic pain show impairment in several related domains. Physical function (e.g., mobility, ability to engage in usual activities) is greatly affected by chronic pain in the general population.[25] Initial studies from this group also suggest that HIV-infected individuals with ''pain today'' have up to 10 times greater odds of impaired physical function.[4] The prevalence of chronic pain increases with age,[26] and the high level of comorbidity between chronic pain and mental illness including depression,[25] anxiety,[27] and substance use[28,29] has been well-established. There is also an association between chronic pain and medical comorbidities, suggesting that individuals with chronic pain have a worse overall health state than individuals without chronic pain.[27]

Therefore, we hypothesized that in the current study of individuals with HIV, those with at least mild pain for more than 3 months on the BCPQ would be older and more functionally impaired (EuroQOL[30]); report a lower overall health state (EuroQOL); and be more likely to have depression (PHQ-9[31]), anxiety (PHQ-anxiety[32]), and use illicit substances (ASSIST[33]). The PRO measures also included a question on pain (EuroQOL), which would be expected to correlate with a positive response to the BCPQ. Finally, we conducted exploratory analyses of the relationship between chronic pain and adherence to HIV antiretroviral therapy (AACTG[34]). All measures used are well validated, and used extensively in HIV-infected patients. Measures were dichotomized so as to use clinically meaningful cut-points and to combine categories with few

Table 1. Measures Used to Quantitatively Evaluate the Brief Chronic Pain Questionnaire

Factor	*Source for measure*	*Variable type*	*Time frame*	*Values*
Physical function	EuroQOL Mobility and Usual Activities questions	Dichotomous	Today	No problem vs. somewhat/unable
Overall health state	EuroQOL Thermometer	Continuous	Today	0 (worst overall health state)–100 (best overall health state)
Pain	EuroQOL pain	Dichotomous	Today	None vs. moderate/extreme
Depression	PHQ-9	Dichotomous	2 weeks	<10 (mild) vs. ≥ 10 (moderate-severe)
Anxiety	PHQ-Anxiety	Dichotomous	4 weeks	No anxiety vs. anxiety/panic
Substance use	ASSIST	Dichotomous	3 months	Use of any illicit substance other than marijuana (opiates, cocaine, methamphetamine, intravenous drug use)
Antiretroviral adherence	AACTG	Dichotomous	2 weeks	No missed doses vs. any missed doses
Consistent pain, depression, anxiety, functional impairment	Pain on 2/2 questionnaires >3 months apart	Dichotomous	18 months	Yes vs. no

PHQ, Patient Health Questionnaire; ASSIST, Alcohol, Smoking, and Substance Involvement Screening Test; AACTG, Adult AIDS Clinical Trials Group adherence questionnaire.

Table 2. Relationship Between the Brief Chronic Pain Questionnaire and Other Variables

Cross-sectional measures	*Chronic pain*[a] N = *30*	*No chronic pain*[a] N = *70*	p-*value*[b]
Age (median, IQR)	49 (39–55)	45 (36–53)	0.23
Impaired mobility	13 (43%)	8 (12%)	0.001
Impaired usual activities	14 (47%)	8 (12%)	< 0.001
Health state thermometer (median, IQR)	70 (51–80)	84 (70–98)	0.002
Pain	24 (80%)	18 (27%)	< 0.001
Depression	9 (30%)	10 (15%)	0.10
Anxiety	13 (43%)	7 (10%)	< 0.001
Substance use	2 (7%)	3 (4%)	0.64
Suboptimal antiretroviral therapy adherence	9 (33%)	16 (26%)	0.61
Repeated reports of measure[c]	*Chronic pain* N = *30*	*Acute pain* N = *12*	p-*value*[a]
Pain	15 (65%)	3 (33%)	0.13
Depression	4 (17%)	1 (11%)	1.000
Anxiety	6 (26%)	2 (25%)	1.000
Impaired mobility	6 (26%)	0 (0%)	0.30
Impaired usual activities	7 (30%)	0 (0%)	0.15

[a]''Chronic pain'' is defined as at least mild pain for >3 months based on the Brief Chronic Pain Questionnaire (BCPQ); ''No chronic pain'' is defined as pain of less than mild severity, no pain, or pain of any severity for <3 months.

[b]Participants with and without chronic pain were compared using the Wilcoxon rank sum test for continuous variables and the Fisher's exact test for categorical variables.

[c]Presence of positive result on measure (e.g., ''pain today'') over two points in time (two measures >3 months apart within 18 months with a ''positive'' result).

Missing values: impaired mobility, no chronic pain 3; impaired usual activities, no chronic pain 4; health state thermometer, chronic pain 1, health state thermometer, no chronic pain 8; pain, no chronic pain 3; depression, no chronic pain 3; substance use, no chronic pain 3; suboptimal adherence, no chronic pain 3; pain, chronic pain 7; depression, chronic pain 7; anxiety, chronic pain 7; impaired mobility, chronic pain 7; impaired usual activities, chronic pain 7; pain, acute pain 3; depression, acute pain 3; anxiety, acute pain 4; impaired mobility, acute pain 4; impaired usual activities, acute pain 3.

participants, as we have done in previous studies.[3] Table 1 summarizes the various PRO measures used to test the BCPQ.

First we examined the cross-sectional relationship between the BCPQ and the aforementioned PROs (depression, anxiety, etc.). Second, PROs assess *current* symptoms (e.g., pain ''today'' or depressive symptoms in the past 2 weeks). As the BCPQ queries *chronic* pain over a 3-month timeframe, we conducted additional analyses to see whether BCPQ-measured chronic pain correlated with repeated reports of pain on the EuroQOL. This was operationally defined as 2/2 instances of pain >3 months apart within the prior 18 months. We performed similar exploratory analyses for depression, anxiety, and impaired mobility/usual activities.

For all analyses, participants with and without chronic pain were compared using the Wilcoxon rank sum test for continuous variables and the Fisher's exact test for categorical variables.

This study was approved by the University of Alabama at Birmingham Institutional Review Board.

Results

Among 100 participants, 25% were female, the mean age was 45 (SD 12), 63% were African American, 27% were publicly insured, 41% were uninsured, the median $CD4^+$ T cell count was 572 cells/mm^3 (interquartile range 307–788), and 82% had an undetectable viral load. Of 100 participants, 30 had chronic pain based on the BCPQ. Of individuals with chronic pain, three (10%) reported mild chronic pain, 19 (63%) moderate, six (20%) severe, and two (7%) very severe. As a check of internal consistency, no participants in the pain severity ''none'' group reported having pain in the past 3 months.

In the cross-sectional analysis, participants with chronic pain were more likely than participants without chronic pain to have impaired mobility (43% vs. 12%, $p = 0.001$), difficulty with usual activities (47% vs. 12%, $p < 0.001$), lower overall health state (70 vs. 84, $p = 0.002$), pain today (80% vs. 27%, $p < 0.001$), and anxiety (43% vs. 10%, $p < 0.001$) (Table 2). Additionally, the PHQ-9 threshold for depression was more commonly met among participants with chronic pain, although this did not reach statistical significance (30% vs. 15%, $p = 0.10$). Other tests of association fell considerably short of statistical significance. These included tests of association between BCPQ-identified chronic pain and advanced age (49 vs. 45, $p = 0.23$), substance use (7% vs. 4%, $p = 0.64$), and suboptimal antiretroviral treatment (ART) adherence (33% vs. 26%, $p = 0.6$).

Just 42 participants had two PROs >3 months apart within 18 months, and were therefore included in the analysis of repeated reports of pain, depression, anxiety, and impaired mobility/usual activities. No statistically significant relationships were found in these analyses. Although not attaining statistical significance, the most suggestive relationships were between BCPQ-identified chronic pain and reporting the following twice in the preceding 18 months: pain ''today'' (65% vs. 33%, $p = 0.13$), impaired mobility (26% vs. 0%, $p = 0.30$), and impaired usual activities (30% vs. 0%, $p = 0.15$). No relationship was observed between the BCPQ and repeated reports of depression and anxiety (Table 2).

Discussion

This is the first study to quantitatively investigate the BCPQ in any clinical population, including HIV-infected patients. Because, for example, many but not *all* patients with

chronic pain have depression, we did not expect to see a 100% correlation between the BCPQ and the other instruments investigated. Rather, in support of construct validity, we looked for trends across instruments. For several of the measures tested, the BCPQ correlated as hypothesized (mobility, problems with usual activities, overall health state, pain today, anxiety, depression). Some fell short of statistical significance (age, substance use, and suboptimal ART adherence), although the direction of the findings typically aligned with hypothesized expectations. Notably, this group has previously found an association between pain and ART adherence in individuals with psychiatric illness and/or substance abuse, but not in individuals with pain alone. However, the present study was not powered to detect this association, and did not address differences between individuals with and without psychiatric illness/substance abuse. Therefore, the present results are consistent with prior findings. In analyses focused on measures over time (including repeated reports of pain ''today,'' depression, and anxiety over the prior 18 months) findings were consistent with cross-sectional results, but did not achieve statistical significance.

This study offers initial evidence of the BCPQ's potential utility in identifying persons with chronic pain. Additionally, its brevity makes it well suited for time-constrained clinical and research settings. We suggest that the BCPQ may serve as a simple and efficient method of preliminarily identifying patients with chronic pain. Persons reporting at least mild pain for greater than 3 months on the BCPQ would require assessments of functional impairment using more detailed instruments that assess pain's impact (e.g., Brief Pain Inventory) and clinical assessments for common comorbidities such as depression and anxiety.

This work has limitations. The sample reflects a population from a single, well-resourced HIV clinic in the Southeastern United States. These results ideally should be replicated in other HIV care settings. Additionally, although cross-sectional analyses were adequately powered ($n = 100$), analyses focused on repeated symptom assessments over time ($n = 42$) were exploratory and future studies with larger samples would be an appropriate next step.

Although these limitations do apply, the BCPQ is strengthened by the decades-long use of one of its two questions in the SF-8 (''How much bodily pain have you had during the last week?'') and by the preceding study in 2,000 healthy Norwegians.[11] Its participant burden is extremely low, and prior qualitative work found that it was understandable and acceptable to individuals with HIV.[13] As previously noted, instruments such as the SF-36 often undergo decades of validity testing but are often used for research and clinical purposes during that process. Therefore, these data provide support for HIV clinicians and researchers who wish to begin using the BCPQ. Future studies using the BCPQ will enable investigation of chronic pain's prevalence among individuals with HIV and the relationship between chronic pain and HIV behavioral and clinical outcomes.

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Author Disclosure Statement

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