PAIN® 154 (2013) 2860–2866

www.elsevier.com/locate/pain

Longitudinal relationships between anxiety, depression, and pain: Results from a two-year cohort study of lower extremity trauma patients

Renan C. Castillo [a,b,*], Stephen T. Wegener [a,b], Sara E. Heins [a], Jennifer A. Haythornthwaite [c], Ellen J. MacKenzie [a], Michael J. Bosse [d], the LEAP Study Group [1]

[a] Department of Health Policy and Management, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA
[b] Department of Physical Medicine and Rehabilitation, Johns Hopkins University, Baltimore, MD, USA
[c] Department of Psychiatry & Behavioral Sciences, Johns Hopkins University, Baltimore, MD, USA
[d] Department of Orthopaedic Surgery, Carolinas Medical Center, Charlotte, NC, USA

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

ARTICLE INFO

Article history:
Received 29 May 2013
Received in revised form 6 August 2013
Accepted 22 August 2013

Keywords:
Pain etiology
Persistent pain
Structural equation modeling

ABSTRACT

Previous studies have shown that pain, depression, and anxiety are common after trauma. A longitudinal relationship between depression, anxiety, and chronic pain has been hypothesized. Severe lower extremity trauma patients ($n = 545$) were followed at 3, 6, 12, and 24 months after injury using a visual analog "present pain intensity" scale and the depression and anxiety scales of the Brief Symptom Inventory. Structural model results are presented as Standardized Regression Weights (SRW). Multiple imputation was used to account for missing data. A single structural model including all longitudinal pain intensity, anxiety symptoms, and depression symptoms time-points yielded excellent fit measures. Pain weakly predicted depression (3–6 months SRW = 0.07, $P = .05$; 6–12 months SRW = 0.06, $P = .10$) and anxiety (3–6 months SRW = 0.05, $P = .21$; 6–12 months SRW = 0.08, $P = .03$) during the first year after injury, and did not predict either construct beyond 1 year. Depression did not predict pain over any time period. In contrast, anxiety predicted pain over all time periods (3–6 months SRW = 0.11, $P = .012$; 6–12 months SRW = 0.14, $P = .0065$; 12–24 months SRW = 0.18, $P < .0001$). The results suggest that in the early phase after trauma, pain predicts anxiety and depression, but the magnitude of these relationships are smaller than the longitudinal relationship from anxiety to pain over this period. In the late (or chronic) phase after injury, the longitudinal relationship from anxiety on pain nearly doubles and is the only significant relationship. Despite missing data and a single item measure of pain intensity, these results provide evidence that negative mood, specifically anxiety, has an important role in the persistence of acute pain.

1. Introduction

Persistent pain is a major public health problem, contributing to high levels of lost productivity [44], disability [10,31], and utilization of health services [29,30,33]. Recent work investigating the persistence of pain beyond the period of healing after an injury [12,13,41,43] or surgery [26,28] implicate a complex interplay between predisposing and evolving biological [20,51] and psychosocial processes in the perpetuation of pain and disability [22,34].

Negative emotions, such as anxiety and depression, increase risk for postoperative and postinjury pain [23,26] as well as new-onset chronic pain [21]. The persistence of pain over time also contributes to the exacerbation of these negative emotions, which is in part related to the severity of pain [17], and these emotions also contribute to deterioration in physical function and poor response to pain management [34]. The interrelatedness of pain, distress, and physical function are difficult to untangle because many studies are cross-sectional, prospective over short periods, or study individuals who already are experiencing persistent pain. Data on the longitudinal and structural relationships among pain, anxiety, and depression can provide key descriptive information and serve as a guide for both the development and timing of effective therapies to improve function and quality of life after injury.

As part of a larger prospective cohort study of lower extremity trauma patients [8,36], we previously examined the longitudinal relationships of both pain intensity and negative mood on function over the first 2 years after traumatic injury [49]. We found that both pain intensity and negative mood were relatively stable over these 2 years, and that higher levels of negative mood had a stable longitudinal relationship with lower levels of function across these first 2 years. On the other hand, the ability of pain intensity to

* Corresponding author. Address: Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, 624 North Broadway, HH 544, Baltimore, MD 21205, USA. Tel.: +1 410 614 4024; fax: +1 410 614 2797.
E-mail address: rcastill@jhsph.edu (R.C. Castillo).
[1] See Appendix.

0304-3959/$36.00
http://dx.doi.org/10.1016/j.pain.2013.08.025

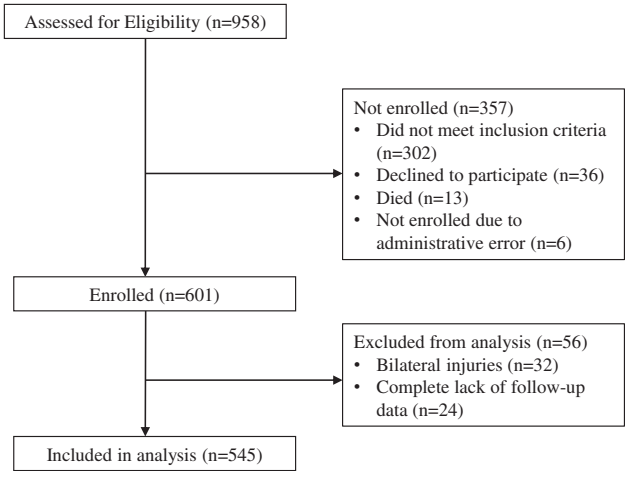
predict function decreased over time. We also found that function did not appear to have any significant longitudinal relationships with pain intensity, depression symptoms, or anxiety symptoms. Though we did not have the sample size to fully examine the longitudinal relationship between all 4 of these variables in a single model, we found that both depression symptoms and anxiety symptoms mediated about half of the relationship between pain intensity and function over the first year of recovery, and nearly all of this relationship over the second year of recovery.

Here we focus on the longitudinal relationship between pain intensity and negative mood among lower extremity trauma patients. On the basis of our prior results regarding the stability of both of these factors but the increasing role of anxiety symptoms and depression symptoms in the chronic phase, we posited that there may also exist an evolving relationship between the 2 factors. The literature has suggested that can pain predict negative mood, and that negative mood may predict the persistence of pain. In this analysis, we hypothesized that we would observe longitudinal relationships between pain intensity and negative mood and that the nature of these relationships may change as the patient enters the chronic phase of recovery.

2. Materials and methods

2.1. Study population and procedures

Participants in the current analysis constitute a subgroup of a larger study conducted to assess the outcomes of amputation or reconstruction after limb-threatening lower extremity trauma. The overall functional, clinical, and psychological outcomes in this population have been described in detail in previous publications [8,14,36,37,49]. This study group included patients 16 to 69 years old who were admitted to 8 level I trauma centers for treatment of high-energy trauma below the distal femur. Excluded were patients with a Glasgow Coma Scale score of <15 at 21 days after hospitalization or discharge [46], spinal cord deficit, or third-degree burn. Also excluded were patients transferred more than 24 h after the injury, subjects who did not speak English or Spanish, patients with a documented psychiatric disorder, and patients on active military duty. We assessed 958 patients for eligibility. Of these patients, 302 did not meet the inclusion criteria, 36 declined to participate, 13 died, and 6 were not enrolled as a result of administrative error, resulting in a final enrollment of 601 participants. For the present analysis, 32 participants with bilateral injuries who met the study criteria were excluded, as well as 24 participants with a complete lack of follow-up data (ie, they were enrolled at hospital discharge but could not be located subsequently).



Subjects were evaluated at baseline (before hospital discharge) and at 3, 6, 12, and 24 months after injury. At each time point, participants were evaluated by an orthopedic surgeon to ascertain complications and limb status, by a physical therapist to ascertain impairment, and by a research nurse to assess the participants' perceptions of functional outcome. Patient-reported outcomes were collected using structured interviews by trained research coordinators at each site. The study was approved by the institutional review board at the coordinating center and at each study site. Informed consent was obtained from all study participants.

2.2. Characterizing participants and their injuries

A number of demographic and injury characteristics have been shown to drive both pain and psychological distress in this population [8,13,37]. We controlled for 9 predictors collected at baseline that have been consistently found to predict outcomes in this population: sex, education, age, length of stay for the initial hospitalization, injury severity, amputation status, pain intensity, self-efficacy for return to work, and social support at time of discharge from the initial hospitalization [7]. Injury severity was measured by the Injury Severity Score (ISS) [2], and length of stay was measured in days. Social support was measured by a modified version of the Inventory of Socially Supportive Behaviors, which measured available support in terms of tangible assistance, directive guidance and emotional support [3,45]. Self-efficacy measured how confident participants were (at the time of hospital discharge) in their ability to resume their major life activity [18,36].

2.3. Outcome measures

Pain intensity was measured at 3, 6, 12, and 24 months using a visual analog scale [47]. Before the examination by the physical therapist, participants were asked to place a mark on a 10-cm line that best described their present level of pain. The line was anchored with the descriptors "no pain at all" on one end and "unbearable pain" on the other end. A continuous score was derived by measuring the distance of the mark (mm) from the lower end of the scale (range 0–100).

Psychological distress was also measured at 3, 6, 12, and 24 months using the Brief Symptom Inventory (BSI) [15], a 53-item abbreviated version of the SCL-90-R (Symptom Checklist) [16]. The BSI consists of 9 primary symptom scales (ie, Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism) and 3 global scales (ie, the General Severity Index, the Positive Symptom Distress Index, and the Positive Symptom Total) [15]. The BSI has demonstrated good to excellent reliability and validity [9]. In this data set, the Cronbach's alpha coefficients were 0.78 to 0.92 for each of the subscales and 0.98 for the GSI global scale at 24 months after injury. Test–retest reliability coefficients ranged from 0.68 to 0.91 for the 9 BSI subscales and 0.80 to 0.90 for the 3 global scales [15].

2.4. Latent variables

From the existing BSI domains, we constructed 2 latent variables for the constructs of depression and anxiety, as has been reported previously [49]. These 2 aspects of psychological distress were chosen because of the significant body of literature showing their relevance to pain and function. The BSI subscales for depression and interpersonal sensitivity were used to construct a latent variable: depression symptoms. The interpersonal sensitivity subscale was included as these subscale items also reflect signs and symptoms of depression (eg, your feelings being easily hurt, feeling inferior to others). Similarly, the anxiety and obsessive-compulsiveness