Risk Factors for Continued Opioid Use One to Two Months After Surgery for Musculoskeletal Trauma

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Background: The aim of this study was to determine factors associated with self-reported ongoing use of opioid medication one to two months after operative treatment of musculoskeletal trauma.

Methods: Operatively treated patients (n = 145) with musculoskeletal trauma were evaluated one to two months after surgery. Patients indicated if they were taking opioid pain medication and completed several psychological questionnaires: the Center for Epidemiologic Studies Depression Scale, the Pain Catastrophizing Scale, the Pain Anxiety Symptoms Scale, and the Posttraumatic Stress Disorder Checklist, civilian version. The Numeric Rating Scale was used to measure pain intensity. Disability was measured with use of the Short Musculoskeletal Function Assessment Questionnaire and injury severity was measured with use of the Abbreviated Injury Scale.

Results: Patients who scored higher on the catastrophic thinking, anxiety, posttraumatic stress disorder, and depression questionnaires were significantly more likely ($p < 0.001$) to report taking opioid pain medications one to two months after surgery, regardless of injury severity, fracture site, or treating surgeon. The magnitude of disability as measured by the Short Musculoskeletal Function Assessment score was significantly higher ($p < 0.001$) in the patients who reported using opioids (40 points) compared with those who reported not using opioids (24 points). A logistic regression model not including pain intensity found that the single best predictor of reported opioid use was catastrophic thinking (odds ratio, 1.12 [95% confidence interval, 1.07 to 1.18]), which explained 23% of the variance ($p < 0.001$).

Conclusions: Patients who continue to use opioid pain medication one to two months after surgery for musculoskeletal trauma have more psychological distress, less effective coping strategies, and greater symptoms and disability than patients who do not take opioids, irrespective of injury, surgical procedure, or surgeon.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

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Opioids are prescribed to reduce pain intensity and disability related to pain. The use of opioids for persistent or chronic non-cancer pain is debated given substantial evidence that they are associated with greater pain intensity, greater pain-related disability, and reduced quality of life[1-3]. Less is known about the effectiveness of opioids in the subacute recovery phase after operative fracture treatment.

In the United States, in contrast with many other parts of the world, most patients take opioids after fractures[4]. Opioid prescription in the United States is increasing, and it is notable that a large percentage of the world's opioid consumption is accounted for by the United States[5,6]. A study of patients recovering from operative fixation of an ankle fracture found that Dutch patients take far fewer opioids, but report similar pain intensity and satisfaction with pain relief compared with patients in the United States[7]. Considering all patients regardless of country, those who took opioids were, on average, less satisfied with pain relief than patients who took non-opioid analgesics[7]. To our knowledge, the scientific data addressing variation in opioid use and satisfaction with pain relief after

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orthopaedic surgery are limited largely to studies that address the ability of ancillary medical interventions to reduce opioid use.

In the original study that created the data set used in this article, pain intensity one to two months after fracture fixation was related to catastrophic thinking (irrational thinking envisioning the worst-case scenario or outcome) and the continued use of opioids rather than the bone that was fractured or injury severity. Pain intensity with activity five to eight months after fracture fixation was much more strongly associated with catastrophic thinking and continued opioid use one to two months after surgery than it was to injury severity. The use of opioids and increased catastrophic thinking early in the recovery were associated with increased pain with activity later on during recovery. Disability was also most strongly associated with catastrophic thinking, but injury severity was also a factor, particularly between five and eight months after injury.

If future studies confirm that opioids are associated with greater pain intensity and disability after fracture fixation, this will add to the already numerous reasons to be cautious with opioids. Opioids have a number of adverse effects, including nausea, vomiting, sedation, constipation, respiratory depression, and hyperalgesia[8,9]. In addition, opioids have other negative consequences including addiction, physical dependence, and tolerance. In 2008, poisoning became the leading cause of injury death in the United States. Nearly nine of ten poisoning deaths are caused by drugs and more than 40% involve opioid analgesics[10]. In one study, patients prescribed opioids for acute pain had an adjusted hazard ratio risk of 6.64 of death from an overdose of opioid pain medication[11]. Addiction is a multidimensional disease and most common in individuals who are biologically (male and younger adults) and psychosocially (stress and mental illness) vulnerable[8,12-15]. Prescription opioid analgesic abuse represents a growing and substantial economic burden and was estimated to be $8.6 billion in the United States in 2001[16]. A recent report found a correlation between sales of prescription opioids and opioid-related drug overdoses treated in emergency departments[17].

We are looking for options to help optimize our patients' postoperative comfort and activity level. Recent studies identified that psychological factors (catastrophic thinking in particular) are strongly associated with pain intensity and disability in patients recovering from minor hand surgery[18] and musculoskeletal trauma[19], and these studies raise promising alternatives. These studies are consistent with the findings of Ip et al., who systematically reviewed twenty-one studies of 7813 patients undergoing musculoskeletal surgery and found psychological distress to be strongly associated with postoperative analgesic consumption along with the type of surgery and patient age[20]. Moreover, catastrophic thinking was predictive of postoperative pain and analgesic use in patients undergoing lumbar fusion surgery[21]. Finally, preoperative anxiety and catastrophic thinking are associated with the development of chronic post-surgical pain[22]. With respect to persistent or chronic non-cancer pain, studies consistently find that prescription of opioid pain medication is associated more strongly with pain behaviors and mental health disorders than with pathophysiology[23-27].

We are interested in the relationship between psychological factors and self-reported opioid use at the subacute stage between one and two months after surgery when recovery is well established. If such an association is identified and is confirmed by other studies, it raises the possibility that treatment of psychological distress and ineffective coping strategies might be additive and perhaps even more fruitful than the prescription of opioids for reducing pain intensity and disability after injury or surgery. Requests for opioids after an appropriate period of recovery might represent a helpful indicator of the potential to benefit from psychosocial interventions.

The aim of this study is to assess factors associated with self-reported continued use of opioid pain medication one to two months after musculoskeletal trauma. Our primary null hypothesis is that there will be no association among psychological factors and self-reported use of opioids one to two months after musculoskeletal trauma while accounting for demographics.

Materials and Methods

The human research committee approved a protocol for the secondary use of data from an existing database of a previously approved prospective study regarding the relationship of psychological factors to pain intensity and disability after surgery for musculoskeletal trauma[19]. All English-speaking patients who were eighteen years of age or more with operatively treated musculoskeletal trauma were eligible. We excluded patients with pre-injury evidence of maladaptive illness behavior or greater infirmity so that we could study human illness behavior among patients with relatively untested adaptation and resiliency. The specific exclusion criteria for the initial study included: major medical comorbidities expected to worsen in the next six months such as cancer and major heart conditions; comorbid chronic pain condition; change in antidepressant medication regimen after injury; psychosis, bipolar disorder, or active substance dependence; secondary gain such as active litigation or a Workers' Compensation dispute; injury affecting cognitive and motor functions; and cognitive deficiency limiting the ability to complete questionnaires.

We used the cross-sectional data of all patients (n = 145) who completed a set of questionnaires and were asked if they were still using opioids one to two months after surgery.

The questionnaires used in this study were the following. The Center for Epidemiologic Studies Depression Scale (CES-D[28]) measured symptoms of depression and had twenty items evaluated on a 4-point Likert scale from 0 to 3 points. A total score is obtained by adding all items, of which four are reversely scored. A score above 16 points was used as an arbitrary threshold for depressive disorder. The Pain Catastrophizing Scale (PCS[29]) measured ineffective coping strategies in response to nociception and had thirteen items evaluated on a 4-point Likert scale from 0 to 3 points. A total score is obtained by adding all items. The Pain Anxiety Symptoms Scale (PASS-20[30]) measured symptoms of anxiety and had twenty items evaluated on a 6-point Likert scale from 0 to 5 points. A total score is obtained by adding all items. The Posttraumatic Stress Disorder (PTSD) Checklist, civilian version (PCL-C[31]), measured symptoms of posttraumatic stress disorder and had seventeen items measured on a 5-point Likert scale from 1 to 5 points. A total score is obtained by adding all items. We used an arbitrary threshold of 33 points for the provisional diagnosis of posttraumatic stress disorder based on an algorithm following the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR)[32] criteria. The Short Musculoskeletal Function Assessment Questionnaire (SMFA[33]) was used to measure musculoskeletal disability and had forty-six items evaluated on a 5-point Likert scale from 1 to 5 points. A total score is obtained by adding all items and then is transferred to a range from 0 to 100 points with use of the formula ([actual raw score − lowest possible raw score]/possible range of raw score) × 100. A higher score indicates greater disability. The Numeric Rating Scale (NRS) for pain was used to assess pain at rest and with activity. This is an 11-point-item scale from 0 points, indicating no pain, to 10 points, indicating the worst pain ever.

Injury severity was measured with the Abbreviated Injury Scale (AIS 2005)[34]. Scores range from 1 to 6 points, with the most severe fatal injuries given 6 points on the basis of severity and anatomic descriptors. Only musculoskeletal AIS scores were used in this study. When patients had multiple musculoskeletal injuries and thus multiple musculoskeletal AIS scores, the highest AIS score was used.

Statistical Analysis

A post hoc power analysis using G*Power software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) indicated that a sample of 145 patients with forty cases would provide >95% statistical power to detect an effect size of 0.9 (based on the means of the best predictor) and a variance inflation factor of 1.3[35].

In a bivariate analysis, continuous explanatory variables (age, catastrophic thinking, anxiety, depression, and posttraumatic stress disorder) and response variables (pain at rest, pain with activity, and disability) were compared to determine the association with the main response variable (opioid use one to two months after injury) using an independent t test. Categorical explanatory variables (sex, fracture site [upper or lower extremity], treating surgeons, primary economic provider status, work-related injury, prior orthopaedic injuries, prior orthopaedic surgeries, injury severity according to AIS, single or multiple injuries, arbitrary threshold score for posttraumatic stress disorder on the PCL-C, arbitrary threshold score for depression on the CES-D) were compared between cohorts using the chi-square test (Fisher exact or Pearson chi-square, depending on the expected count). Significance was set at $p < 0.05$.

A multivariable backward logistic regression model was created to account for confounding between the explanatory variables. Variables with $p < 0.10$ in the bivariate analysis were entered in the model. This is a common cutoff value for inclusion of variables in regression modeling when the total number of study subjects is small. We ran two models, one that did not use response variables (e.g., pain, disability, and opioid use) as explanatory variables and one that included pain as one of the explanatory variables.

The Nagelkerke R-square and the Hosmer-Lemeshow tests were used for the overall model to assess study power and goodness of fit. Odds ratios (ORs) were calculated with the 95% confidence interval (95% CI).

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Results

Bivariate Analysis

Forty patients (28%) reported using opioid pain medication one to two months after injury, including twenty of seventy-six women and twenty of sixty-nine men. Thirty-five patients (24%) met our arbitrary threshold for an estimated diagnosis of major depressive disorder as measured on the CES-D and forty-two patients (29%) met our arbitrary threshold score on the PCL-C for an estimated diagnosis of posttraumatic stress disorder. The mean PCS (catastrophic thinking), mean PASS-20 (anxiety), mean PCL-C, and mean CES-D (depression) scores were significantly higher in patients using opioids ($p < 0.001$).

There was a strong significant correlation (R-square) ($p < 0.001$ for all) between PCS and CES-D (0.7), between NRS and both PCS (0.7) and CES-D (0.5), and between SFMA and both PCS (0.7) and CES-D (0.6).

Patients were more likely to report that they were still taking opioid pain medication if they met our arbitrary threshold scores on the PCL-C ($p = 0.002$) and CES-D ($p = 0.006$) one to two months after surgery. Patients still taking opioid medication one to two months after surgery had greater pain intensity (at rest and with activity) and disability ($p < 0.001$). Injury severity and fracture site were not related with continued opioid use ($p = 0.08$) (see Appendix).

Multivariable Analysis

When the four explanatory variables that met the criteria for inclusion (catastrophic thinking, symptoms of anxiety, symptoms of posttraumatic stress disorder, and symptoms of depression) were entered into a backward logistic regression model, catastrophic thinking (OR, 1.12 [95% CI, 1.07 to 1.18]) was the only factor retained and it explained 23% of the variation in opioid use ($p < 0.001$). This analysis was repeated using our arbitrary threshold values on the PCL-C and CES-D, instead of the scores, and the results were identical. A model that included pain with activity explained 34% of the variance in opioid use ($p < 0.001$).

Discussion

Despite the fact that most musculoskeletal injuries are well along in the recovery process one to two months after operative treatment, 28% of our patients continued to take opioid pain medication at this time point. This rate is compared with 25% of patients three months after spine surgery[36] and 6% of patients five months after mastectomy, lumpectomy, thoracotomy, total knee replacement, or total hip replacement[37].

The use of opioid pain medication one to two months after surgery for musculoskeletal trauma was most strongly associated with catastrophic thinking (as measured on the PCS), but also with symptoms of pain anxiety (as measured on the PASS-20), symptoms of depression (as measured on the CES-D), and symptoms of posttraumatic stress disorder (as measured on the PCL-C). Patients meeting our arbitrary threshold values on the PCL-C and CES-D were more likely to still be taking opioid pain medication one to two months after surgery. In other words, better mood and more adaptive coping strategies help patients discontinue opioids after musculoskeletal trauma surgery.

In this study, the mean disability (as measured by the SMFA) and the mean pain intensity were significantly higher in patients still using opioid pain medication one to two months after surgery ($p < 0.001$), irrespective of fracture site or injury severity. This result is consistent with evidence that variations in postoperative acute and chronic pain are best explained by preoperative psychological factors and demographics[20-22]. It is also consistent with the weight of research on persistent or chronic non-cancer pain, which has demonstrated that opioid use is associated with lower self-rated health, greater unemployment, greater use of health-care resources, lower quality of life, and more intense pain[1,38-42].

Given the shortcomings and adverse events associated with opioid medication, greater pain and disability than expected, including requests for opioids one to two months after fracture surgery, should prompt health-care providers to consider the important roles of stress, depressed mood, and ineffective coping strategies in human illness behavior, and to be more prepared to offer a full complement of treatments to help their patients feel better and do more. It seems, at least in the United States, that both patients and surgeons may often look to opioid pain medication as the best or only hope for relief of postoperative pain. The evidence suggests otherwise. Catastrophic thinking is responsive to cognitive behavioral therapy. Providers of musculoskeletal health care, including occupational and physical therapists, can improve the situation by empathetically encouraging patients to talk about the emotional aspects of recovery and by avoiding reinforcement of ineffective coping strategies.

Our study should be considered in light of its limitations. First, this study represented secondary use of data from a prospective cohort study. Second, we used validated measures of symptoms of posttraumatic stress disorder and depression and used arbitrary cutoffs for categorization. The diagnosis of posttraumatic stress disorder or major depression would require a formal evaluation. Third, this study measured cross-sectional, self-reported opioid use as a dichotomous measure and did not address opioid intake with blood tests or other measures. Fourth, the AIS might be inadequate for discriminating injury severity. Relatively few patients had more severe injuries, and our statistical analysis of injury severity may therefore have been underpowered. Fifth, the broad areas of evaluation for enrollment and final evaluation are wide, but reflect the realities of clinical research and are necessary to avoid protocol violations and to satisfy strict human research oversight. Finally, no causal relationships could be inferred and the optimal use of opioid medication was not addressed by this study.

There is strong evidence that a biopsychosocial treatment model reduces pain[43]. This model is established for non-traumatic musculoskeletal pain[44] and, in our opinion, should now be translated to traumatic musculoskeletal pain at all phases of recovery. Addressing psychosocial factors in the early phases of recovery might reduce disability and might improve the outcome of surgical and medical procedures[45]. Interdisciplinary treatment could potentially decrease opioid use and associated adverse consequences. Future research should focus on providing surgeons with effective strategies for recognizing and addressing important psychological factors and appropriately limiting opioid pain medications. We hypothesize that screening for low pain self-efficacy (increased catastrophic thinking), feedback to the patients that improved self-efficacy will reduce pain and disability, familiarity with the basic techniques of cognitive behavioral therapy, and appropriate support from behavioral health professionals for receptive patients can ameliorate pain behavior and can reduce analgesic requirements.

Appendix

eA A table showing the bivariate analyses of opioid medication use one to two months after surgery with regard to categorical explanatory variables and a table showing the bivariate analyses of opioid medication use one to two months after surgery with regard to continuous explanatory variables are available with the online version of this article as a data supplement at jbjs.org. ■

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