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GENERAL ORTHOPAEDICS

Factors associated with persistent opioid use after an upper extremity fracture

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Aims

The increase in prescription opioid misuse and dependence is now a public health crisis in the UK. It is recognized as a whole-person problem that involves both the medical and the psychosocial needs of patients. Analyzing aspects of pathophysiology, emotional health, and social wellbeing associated with persistent opioid use after injury may inform safe and effective alleviation of pain while minimizing risk of misuse or dependence. Our objectives were to investigate patient factors associated with opioid use two to four weeks and six to nine months after an upper limb fracture.

Methods

A total of 734 patients recovering from an isolated upper limb fracture were recruited in this study. Opioid prescription was documented retrospectively for the period preceding the injury, and prospectively at the two- to four-week post-injury visit and six- to nine-month post-injury visit. Bivariate and multivariate analysis sought factors associated with opioid prescription from demographics, injury-specific data, Patient Reported Outcome Measurement Instrumentation System (PROMIS), Depression computer adaptive test (CAT), PROMIS Anxiety CAT, PROMIS Instrumental Support CAT, the Pain Catastrophizing Scale (PCS), the Pain Self-efficacy Questionnaire (PSEQ-2), Tampa Scale for Kinesiophobia (TSK-11), and measures that investigate levels of social support.

Results

A new prescription of opioids two to four weeks after injury was independently associated with less social support (odds ratio (OR) 0.26, $p < 0.001$), less instrumental support (OR 0.91, $p < 0.001$), and greater symptoms of anxiety (OR 1.1, $p < 0.001$). A new prescription of opioids six to nine months after injury was independently associated with less instrumental support (OR 0.9, $p < 0.001$) and greater symptoms of anxiety (OR 1.1, $p < 0.001$).

Conclusion

This study demonstrates that potentially modifiable psychosocial factors are associated with increased acute and chronic opioid prescriptions following upper limb fracture. Surgeons prescribing opioids for upper limb fractures should be made aware of the screening and management of emotional and social health.

Cite this article: *Bone Jt Open* 2021;2-2:119–124.

Keywords: Opioid use, Pain management, Instrumental support, Social support, Trauma surgery, Upper extremity fracture

Introduction

The epidemic of prescription opioid misuse is now a public health crisis in European countries as well as the USA.[1-6] In the UK, opioid-related deaths now comprise the largest contribution to drug-related deaths in the country.[2,7,8] Greater access to opioids, a proliferation of synthetic formulations, liberal prescribing practices, and the overstatement of benefits and understatement of risks by pharmaceutical companies have driven the rise in opioid-related overdose, morbidity, and mortality.[1,2,5,9] A complex interplay of clinical and contextual factors, including mental and social health concerns, make opioid use and misuse a whole person problem affecting those with complex needs, especially in acute care and surgical settings.[9,10]

In musculoskeletal trauma, patients using prescription opioids one to two months after surgery are shown to have greater

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doi: 10.1302/2633-1462.22.BJO-2020-0167.R1

Bone Jt Open 2021;2-2:119–124.

psychological distress, worst-case thinking, and less effective coping abilities compared to those not taking opioids, independent of surgical and injury factors.[11,12] After injury and fracture, continued use of opioids is associated along with psychological factors such as greater pain catastrophization, fear of movement, lower self-efficacy, and long-term disability.[12,13] For those undergoing surgery, preoperative opioid dependence and fracture complexity are important risk factors for postoperative opioid dependence after fracture fixation, however these are not easily modifiable by treating surgeons.[12,14,15]

The primary objective of this study was to evaluate which psychosocial factors are associated with continued opioid use two to four weeks after injury. The secondary objective was to assess which psychosocial factors are associated with continued opioid use at six to nine months. Finally, we evaluated the differences in pain intensity, satisfaction with clinical care and overall services, general health-related quality of life (measured by the EuroQolfive-dimension three-level questionnaire (EQ-5D-3L))[16] and the magnitude of limitations (measured by the Patient Reported Outcome Measurement Instrumentation System Upper Limb Physical Function (PROMIS UE)) between patients using opioids versus those not using opioids two to four weeks after injury.[17]

Methods

Adult patients with isolated shoulder, elbow, or wrist injuries were approached between 1 January 2016, and 31 August 2016 at a UK major trauma centre. Inclusion criteria were fluency in English, an age of 18 years or older, and the ability to provide informed consent. Patients were ineligible if they sustained a concurrent injury involving the same arm in which they had sustained the shoulder, elbow, or wrist fracture or in any region (e.g. as part of complex polytrauma); refracture during recovery from a previous injury; fracture-dislocation; or a fracture around a previous fixation or joint arthroplasty). This is a retrospective, secondary data analysis gathered from a research and ethics committee-approved study.

A total of 775 patients were initially selected. Of these, 31 (4%) declined to participate because of time constraints, four patients died of an unrelated illness before the last measurement interval (six to nine months after injury), and six patients could not be contacted. We included 734 patients in our final selection, of whom 489 (67%) were female, and the mean age of whom was 58.5 years (SD 20.4).

Demographic and clinical details including age, sex, education level, marital, social, and work status, arm dominance, index of multiple deprivation, Charlson Comorbidity Index (CCI), and occurrence of prior arm fractures were collected from each patient. Details of the injury itself, including the location and classification of the injury, whether the fracture was open, high-energy, or had neurovascular compromise, and whether the patient had surgery were gathered from health records. In addition, a broad injury classification was created and defined in Supplementary Table i. Complete demographic and clinical information are detailed in Supplementary Table ii. Mental health measures were captured at baseline (the initial orthopaedic clinic visit at a maximum of one week after the injury). The following measures were collected: Patient-Reported Outcomes Measurement Information System (PROMIS) UE, Computerized Adaptive Testing (CAT), PROMIS Pain Interference (PROMIS PI) CAT, PROMIS Depression CAT, PROMIS Anxiety CAT, PROMIS Emotional Support CAT (PROMIS ES), PROMIS Instrumental Support CAT (PROMIS IS), Pain Catastrophizing Scale (PCS), Pain Self-efficacy Questionnaire (PSEQ-2), Tampa Scale for Kinesiophobia (TSK-11), patient satisfaction with their care providers, patient satisfaction with the hospital services, Likert pain scale, and EQ-5D-3L. These questionnaires were collected on a secure, encrypted, web-based data collection platform (Assessment Centre, Northwestern University, Evanston, Illinois, USA). A description of these patient-reported outcomes is included in Supplementary Table iii.

We recorded the prescription of opioid analgesics from the emergency department, fracture clinic, and inpatient orthopaedic service as well as primary care practitioners, specifically for their upper limb injury. A total of 22 patients (3%) from the entire cohort had existing opioid prescriptions for another condition prior to injury. Of these patients, 17 (2%) had their prescriptions increased to account for their upper limb fracture.

Statistical analysis. We performed descriptive statistics including frequencies and percentages for discrete variables and mean with SD for continuous variables. Bivariate analysis was conducted with independent-samples *t*-tests for continuous variables and chi-squared tests for categorical variables investigating the relationship between demographic variables and mental health measures with opioid use.

The mental health measures were checked for multicollinearity, the phenomenon in which two or more predictor variables in a multiple regression model are highly correlated, meaning one can be linearly predicted from the other with a substantial degree of accuracy. This may be indicated by wide 95% confidence intervals, high standard error and high β, and assessed by partial R2, correlation matrices at less than one week and two to four weeks, and variance inflation factor (VIF). VIF is an index measuring the extent to which variance of estimated regression coefficients and independent variables increase due to collinearity. A correlation greater than 0.75 was considered indicative of multicollinearity and led to the omission of one of two variables with this high correlation i.e. the variable with the largest VIF value (Supplementary Table iv). Sensitivity analysis

demonstrated that omission of variables did not reduce the models' adjusted R2, i.e. the overall ability to predict the outcome variable.

The remaining psychosocial measures and each independent variable correlating with opioid use with $p < 0.10$ in bivariate analysis (Supplementary Table v, Supplementary Table vi), were entered into multivariate regression predicting opioid use. Two regressions were created: one investigating the influencing factors for opioid use at two to four weeks, and one on the factors predicting opioid use at six to nine months. Finally, differences in psychosocial factors, pain intensity, physical function, and general health and satisfaction, were evaluated between opioid users and opioid non-users in bivariate analysis withindependent-samples *t*-tests. A power analysis performed to check sample size for our objective to detect a five-point difference in one of our patient-reported outcome measure (PROM) scores—PROMIS depression—between opioid users and non-users with a SD of 15 in both groups indicated 380 patients would be needed to provide 90% power. All statistical analysis was performed using SAS Version 9.4 (Cary, North Carolina, USA), and statistical significance was set at $p < 0.05$. There were no funding sources for this secondary investigation.

Results

In all, 734 patients were studied in this analysis. Accounting for potential confounding in multivariable analysis, factors independently associated with continued opioid prescription two to four weeks after injury included less social support (odds ratio (OR) 0.26, $p < 0.001$), worker compensation (OR 7.7, $p < 0.001$), greater fracture severity (OR 1.9, $p = 0.018$), less instrumental support (OR 0.91, $p < 0.001$), greater symptoms of anxiety (OR 1.1, $p < 0.001$), and less pain self-efficacy (OR 0.9, $p = 0.041$; $R^2 = 0.57$; Table I).

Accounting for potential confounding in multivariable analysis, factors independently associated with continued opioid prescription six to nine months after injury included less instrumental support (OR 0.9, $p < 0.01$) and greater symptoms of anxiety (OR 1.1, $p = <0.001$; $R^2 = 0.42$, Table II).

In bivariate analysis, patients who were taking opioids two to weeks after injury had lower satisfaction, greater pain interference, greater upper limb specific limitations (lower PROMIS PF UE CAT scores), and lower general health (lower EQ-5D-3L scores) compared to those not taking opioids at this stage (all $p < 0.001$) (Table III).

Table I. Multivariable logistic regression evaluating risk for opioid use at two to four weeks.

Variable	OR (95% CI)	p-value
Marital status		
Single	REF	
Partner/married	1.60 (0.81 to 3.20)	0.180
Separated	0.88 (0.42 to 1.80)	0.740
Social Support		
Alone	REF	
Partner/Friends/Family	0.26 (0.13 to 0.54)	< 0.001
Full/Part-time care	0.43 (0.18 to 1.00)	0.062
Work status		
Retired	REF	
Unemployed	3.40 (0.94 to 12.00)	0.062
Workers comp	7.70 (1.70 to 34.00)	0.007
Working/Homemaker	1.20 (0.70 to 2.00)	0.520
IMD Factor	1.00 (0.99 to 1.00)	0.530
Broad Injury Classification		
Category 1	REF	
Category 2	1.60 (0.88 to 2.80)	0.120
Category 3	1.90 (1.10 to 3.20)	0.018
High-energy injury		
Yes	1.50 (0.81 to 2.80)	0.190
No	REF	
Neurovascular compromise		
Yes	1.20 (0.47 to 2.90)	0.730
No	REF	
Surgery		
Yes	1.10 (0.61 to 2.00)	0.750
No	REF	
Prior non-dominant side fracture		
Yes	0.85 (0.44 to 1.70)	0.630
No	REF	
Mental health measures		
PROMIS Depression	1.00 (0.99 to 1.00)	0.360
PROMIS Anxiety	1.10 (1.00 to 1.10)	0.001
PROMIS Instrumental Support	0.91 (0.89 to 0.94)	< 0.001
TSK-11	1.00 (0.97 to 1.10)	0.600
PCS	1.00 (0.97 to 1.10)	0.310
PSEQ	0.90 (0.82 to 1.00)	0.041

CI, confidence interval; IMD, Index of Multiple Deprivation; IMD, indices of multiple deprivation; OR, odds ratio; PCS, Pain Catastrophising Scale; PROMIS, Patient-Reported Outcome Measurement Instrumentation System; PSEQ, Pain Self-efficacy Questionnaire; TSK-11, Tampa Scale for Kinesiophobia.

Discussion

Based on the association between opioid use and psychosocial factors, it is important to discern mental and social health opportunities for enabling comfortable and expedient recovery after injury. The failure to appreciate a patient's emotional and social needs may lead to misdiagnosis of these factors as part of the pathophysiology and, further, mistreatment with opioids. While there has been an increase in initiatives by orthopaedic organizations to decrease and eliminate opioid prescriptions, these efforts rarely incorporate psychosocial factors which may contribute to their lack of efficacy.[18,19] In this analysis, we confirmed that opioid use is associated with worse mental and social health.

The findings of this study can be considered in light of some limitations. First, this study was performed at a single centre in the UK and therefore the results might be specific to our population. Second, while we were

Table II. Multivariable logistic regression evaluating risk for opioid use at six to nine months.

Variable	OR (95% CI)	p-value
Marital status		
Single	REF	
Partner/Married	1.20 (0.40 to 3.70)	0.730
Separated	0.71 (0.31 to 1.60)	0.410
Social support		
Alone	REF	
Partner/Friends/Family	0.46 (0.16 to 1.30)	0.130
Full/Part-time care	1 (N/A*)	0.970
Work status		
Retired	REF	
Unemployed	0.82 (0.31 to 2.20)	0.690
Workers comp	1.10 (0.40 to 3.10)	0.840
Working/Homemaker	0.57 (0.26 to 1.20)	0.160
IMD Factor	1.00 (0.99 to 1.00)	0.660
High-energy injury		
Yes	0.62 (0.29 to 1.30)	0.210
No	REF	
Neurovascular compromise		
Yes	1.80 (0.70 to 4.90)	0.210
No	REF	
Mental health measures		
PROMIS Depression	0.99 (0.96 to 1.00)	0.780
PROMIS Anxiety	1.10 (1.00 to 1.10)	0.004
PROMIS Instrumental Support	0.90 (0.86 to 0.95)	< 0.001
TSK-11	1.00 (0.97 to 1.10)	0.260
PCS	0.97 (0.92 to 1.00)	0.23
PSEQ	0.96 (0.83 to 1.10)	0.57

*Not enough data.
CI, confidence interval; N/A, not applicable; OR, odds ratio; PCS, Pain Catastrophising Scale; PROMIS, Patient-Reported Outcome Measurement Instrumentation System; PSEQ, Pain Self-efficacy Questionnaire; TSK-11, Tampa Scale for Kinesiophobia.

Table III. Differences in patient-reported outcomes among opioid users and opioid non-users.

Mean outcome score (SD)	Opioid use at 2 to 4 weeks*	
	Not using	Using
PROMIS Depression	49 (9.1)	58 (11)
PROMIS Anxiety	48 (9.0)	58 (9.9)
PROMIS Pain Interference	66 (6.4)	69 (6.6)
PROMIS Emotional Support	57 (7.3)	44 (9.8)
PROMIS Instrumental Support	58 (6.3)	47 (8.5)
PCS	18 (4.5)	24 (8.1)
PSEQ	10 (2.3)	7.1 (2.9)
TSK-11	25 (6.5)	31 (6.3)
Likert Pain Scale	8.4 (1.2)	9.1 (1.1)
PROMIS Upper Limb	25 (6.2)	23 (6.2)
EQ-5D-3L	0.33 (0.32)	0.16 (0.39)
Patient satisfaction with providers	8.8 (1.0)	7.0 (1.9)
Patient satisfaction with hospital	8.3 (1.3)	5.8 (2.1)

*All p-values were < 0.001.
EQ-5D-3L, EuroQol five-dimension three-level questionnaire; PCS, Pain Catastrophizing Scale; PROMIS, Patient Reported Outcome Measurement Instrumentation System; PSEQ-2, Pain Self-efficacy Questionnaire; TSK-11, Tampa Scale for Kinesiophobia.

aware of the patients who had existing opioid prescriptions that were increased to contend with fracture pain (2%) versus those who were opioid naïve, receiving new prescriptions (98%), we did not account for them in our analysis as the proportion of patients was relatively low and therefore unlikely to have a substantial impact on the overall outcome. Third, while we included those undergoing surgical intervention in our analysis, we did not account for those supplied with new opioid prescriptions or modifications of existing opioid prescriptions postoperatively versus those supplied in the emergency department, orthopaedic outpatient setting, or by the general practitioners in the community. The high reliance on postoperative opioid prescriptions is prevalent in the USA and shown to be a dominant factor in opioid dependence.[10,12,15] Nevertheless, surgical rates were relatively low and therefore this aspect was unlikely to impact on our general findings. Fourth, our only measures of pathophysiology were fracture location and AO Type. Additional subdivisions of injury characteristics may uncover the relationship between certain pathologies and opioid use. Fifth, it should be kept in mind that the PROMIS ES and IS scores were not assessed until two to four weeks. This is likely a good time to assess support, after a period of time to recover from and adapt to injury. arlier Eattempts to diagnose and manage social health opportunities, however, might have different results. Additionally, it is important to note that we measured opioid prescriptions, not opioid use. It is unlikely, however, that new opioid prescriptions were given at two-week and six-month clinic visits if patients were not active opioid users at that time. Measures of actual use may have different results, although we feel this risk is small. Finally, we were not able to determine when a prescription was filled; therefore, there may have been a gap between when a script was prescribed and when it was filled. It is possible we may have missed continued opioid use if patients filled old opioid prescriptions several weeks later.

The association of greater symptoms of anxiety and less pain self-efficacy with continued opioid use two to four weeks after injury is consistent with the important influence of mental and social health on pain intensity and satisfaction with pain alleviation, as well as requests for opioids identified in prior studies.[20] Symptoms of anxiety and depression are associated with a second opioid prescription after injury.[20–22] In addition, feelings of loneliness and financial hardship,[23] as well as greater catastrophic thinking in response to nociception,[24] are also associated with ongoing opioid prescriptions.

The finding that worse social support (less patient-reported instrumental support) is associated with continued opioid use six to nine months after injury documents the importance of opportunities for social

health and wellbeing during longer-term recovery from injury. Social health is important in several aspects of a patient's recovery from injury and represents feelings of social support, personal value, belonging, and trust.[25] A study of 1,649 patients with musculoskeletal injury following a road traffic accident found that support from family and friends was associated with less self-reported pain and higher physical component scores of the Short-Form-12 (SF-12) Health Survey.[26] In addition, a study of patients recovering from total hip arthroplasty found that better social health was associated with a greater ability to walk.[27]

The finding that patients who take opioids two to four weeks after an upper limb fracture have worse general health (measured by the EQ-5D-3L) and greater upper limb-specific limitations compared to those who do not take opioids confirms that people taking opioids have difficulty with recovery including problems related to factors other than their pathophysiology, such as psychological distress and unmet social needs (e.g. lack of social support, lack of help from friends/family). Several past studies have similarly demonstrated worse physical function,[28] as well as worse physical and mental quality of life, in patients who take opioids.[29]

There is some debate on the effect of opioid prescription on satisfaction.[30–33] We found that patients continuing to take opioids have worse satisfaction. In the USA, the inclusion of pain management in patient satisfaction scores has tied the management of pain to reimbursement, with concerns that anti-opioid campaigns could be linked to decreased satisfaction and ultimately compensation.[6] Two retrospective studies of 19,566 and 69,985 patients found that patients who are prescribed opioids are more likely to report higher satisfaction with their care.[30,34] On the other hand, programmes which have reduced opioid use and prescriptions in surgical patients have done so without decreasing patient satisfaction.[31,32] For example, a state-wide programme in the USA which reduced opioid consumption by 25% in general surgery patients found no impact on patient satisfaction.[31] In addition, two independent studies of 232 and 97 orthopaedic surgical patients found that opioids actually decreased pain satisfaction and increased pain intensity 24 hours and 14 days after surgery, respectively.[32,35]

While the risk of tying opioid prescriptions to satisfaction ratings in performance-based reimbursement plans is less of an issue in universal healthcare systems, such as the NHS, the assessment of patient experience and satisfaction remains central to quality improvement and national benchmarking.[36] A further advantage of universal healthcare is the opportunity for coordinated efforts between primary and secondary care governed by commission groups in jointly developed strategies, including psychological interventions and social support, to oversee prescription and control.[10] The USA experience of the opioid crisis serves as a call to action, especially as the proportion of patients classified with prolonged opioid prescriptions (roughly one in four patients) in our UK cohort was surprisingly high.[37,38] Structural elements within the NHS around tight prescription control, de-prescribing, a drive to achieve comparable pain relief with non-opioid regimens, regular review of prescriptions, and availability of antidotes such as methadone may buffer the harmful effects of opioids.[1,10,38,39] However, it appears that additional strategies are needed to safeguard against adverse events in the high rates of opioid use in orthopaedic trauma, at least based on this study.[40]

In conclusion, rrespective of the healthcare setting, our findings highlight the underlying need for awareness and education around the whole-person impact of opioid overuse, and opioid-sparing multimodal pain management strategies and validated screening protocols that integrate mental health and social support, coaching, and therapy.[9,38,41] From a public health perspective there is also a call for alignment between pain management and mental health priorities with evidence-based screening and surveillance systems (including predictive modelling solutions) for at-risk individuals.[9,42] Addressing mental and social health is an important aspect of safe and effective alleviation of pain and optimal opioid stewardship.[41,43]

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Supplementary material

Additional tables and a correlation matrix elaborating on the results of our study.

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Funding statement:
- No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

ICMJE COI statement:
- S. E. Lamb was on the Health Technology Assessment (HTA) Additional Capacity Funding Board, HTA End of Life Care and Add-on Studies Board, HTA Prioritisation Group Board, and the HTA Trauma Board.

Ethical review statement:
- The study was approved by the local research and ethics committee (IRAS No. 16/YH/0017).