Prescription Patterns and Risk Factors for Prolonged Opioid Dependence in Elective Anterior Cruciate Ligament Reconstruction in a Military Population

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Background: Limited data are available regarding excessive opioid prescribing in the perioperative period after routine orthopaedic procedures in US military personnel.

Purpose: To examine the demographic profile of the patients receiving these medications and to identify potential risk factors for prolonged opioid use after anterior cruciate ligament reconstruction (ACLR) in the active duty military population.

Study Design: Case-control study; Level of evidence, 3.

Methods: The Military Analysis and Reporting Tool (M2) was used to search the Military Health System Data Repository (MDR) for patients undergoing ACLR from 2012 through 2015 and specifically for active duty personnel with an arthroscopically assisted ACLR (Current Procedural Terminology [CPT] code 29888). Complete opioid prescription filling history was also obtained. This study had 2 primary outcomes: (1) use of opiate analgesics more than 90 days after surgery, representing prolonged opiate prescriptions, and (2) high levels of postoperative opiate use, defined as having filled prescriptions accounting for greater than the 95th percentile of morphine equivalents for patients in the study cohort. Data were analyzed via multivariate regression analysis to identify potential associations with the primary outcomes.

Results: A total of 9474 patients met the inclusion criteria. Median patient age was 27 years, and the sample included 1316 (14%) female and 8158 (86%) male patients. A total of 66 (0.7%) patients had a preoperative diagnosis for substance abuse; 2656 (28%) patients continued to receive opioid prescriptions more than 90 days after surgery, and 502 (5%) patients were in the top 95th percentile of all opioid users within the study cohort. Total preoperative morphine equivalents per day and total perioperative morphine equivalents per day were highly important risk factors for both outcomes, although other demographic factors such as race, sex, and age may play minor roles.

Conclusion: We identified total preoperative morphine equivalents, total perioperative morphine equivalents, sex, and race as potential predictors of prolonged opioid use after ACLR. This information may prove useful in developing a predictive model to identify at-risk patients before surgery. This could help mitigate future misuse or abuse and improve preoperative patient counseling regarding pain management expectations.

Keywords: opioids; ACL reconstruction; opioid use disorders; perioperative risk management; opioid epidemic; big data

Approximately 100 million people in the United States experience chronic pain, and 92 million people use opioids for pain relief.7,9,17 In 2012, for every 100 persons in the United States, 82.5 opioid prescriptions and 37.6 benzodiazepine prescriptions were written by healthcare providers.7,8 The increase in opioid prescribing during this period was not paralleled by an increase in prescriptions for nonsteroidal anti-inflammatory drugs or acetaminophen; between 2000 and 2010, the number of pain management opioid prescriptions increased from 11.3% to 19.6% while nonopioid prescriptions increased from 26% to 29%.7,8

Little knowledge is available regarding perioperative opioid use in the healthy, young, and active population. Accounting for 7.7% of all opioid prescriptions in the United States, orthopaedic surgeons are the third highest prescribers of opioids among physicians,13 after primary care physicians (28.8%) and internal medicine physicians (14.6%).7,17,19,21 A recent study evaluated persistent opioid use after both major and minor surgical procedures.6 At 90 and 180 days postoperatively, the rates of new and persistent

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use showed no significant difference between major and minor surgical procedures. A significant association was seen with a patient history of behavioral or pain disorders, suggesting that persistent use may be predicted preoperatively based on patient characteristics or risk factors.

The US Department of Defense has a closed, egalitarian healthcare system that requires beneficiaries to obtain their care and prescriptions from within this system. Information on all healthcare encounters occurring within the US Military Health System (MHS) is recorded in the MHS Data Repository (MDR), which is accessible through the Management Analysis and Reporting Tool (M2). This database provides medical researchers with a unique opportunity to study injuries. Researchers from a variety of disciplines, including orthopaedic surgery, have used this database. Using the available pharmacy information, we are able to identify filled prescriptions for opioid medications and measure the strength of those medications by converting them into a standardized form: morphine equivalents.

The purposes of this study were 3-fold: (1) to identify rates of opioid use before and after anterior cruciate ligament reconstruction (ACLR), (2) to evaluate postoperative trends in opioid use for 1 year after ACLR, and (3) to identify and describe risk factors for prolonged opioid use after ACLR in an otherwise healthy, young, and active population.

METHODS

The MDR contains patient-specific details on all healthcare encounters for MHS beneficiaries for the past 5 years. After institutional review board approval was granted, M2 was used to search the MDR for all patients undergoing ACLR from January 2012 through December 2015. Patients were included for analysis if they had a single encounter with the Current Procedural Terminology (CPT) code for arthroscopically assisted ACLR (29888) and were active duty military personnel at the time of surgery.

Complete opioid prescription filling history was obtained for the patient population via pharmacy records obtainable through the same system. Previous studies had defined patients as demonstrating "chronic opioid use" if they had filled a prescription preoperatively at 30 to 120 days from surgery or "new persistent opioid use" if they had filled an opioid prescription between 90 and 180 days after a surgical procedure. Preoperative opioid prescriptions (between 180 and 365 days preoperatively), perioperative opioid prescriptions (between 30 days preoperatively and 30 days postoperatively), and prolonged opioid prescriptions (between 90 and 365 days postoperatively) were tracked for all patients in the cohort.

Because the quantity and strength of pills dispensed for any given prescription or drug might vary, we standardized cumulative dosing by converting all opioid prescriptions to morphine milligram equivalents (mme) using official Centers for Disease Control and Prevention opioid prescribing guidelines. Perioperative opioid prescriptions were divided into approximately equal quartiles based on morphine equivalents that ranged from $>0$ to $\leq 7.5$ mme (30.0%), $>7.5$ to $\leq 11.2$ mme (21.2%), $>11.2$ to $\leq 16.7$ mme (23.9%), and $>16.7$ to 184 mme (24.8%).

This study had 2 primary outcomes of interest:

1. Prolonged opioid use, defined as filling a prescription for opioid analgesics more than 90 days after surgery
2. Extreme opioid use, defined as filling a prescription for a quantity of morphine equivalents greater than or equal to the 95th percentile of morphine equivalents for patients who filled prolonged opioid prescriptions

In addition to analyzing rate and duration of preoperative and perioperative opioid use, we analyzed other patient factors for potential associations with prolonged postoperative use. For each patient, basic characteristic and encounter data were recorded including date of surgery, surgical location, age at surgery, sex, race, and military status (active duty, retired, dependent, or other). Preoperative diagnoses for substance abuse disorders were also documented through use of the International Classification of Diseases, Ninth Revision (ICD-9) codes for substance abuse (30400, 30401, 30402, 30403, 30460, 30462, 30463, 30470, 30471, 30472, 30473, 30490, 30491, 30492, 30550, 30551, 30552, 30553, 30590 30591, 30592, and 30593). A comorbid diagnosis of substance abuse disorder was
recorded via the M2 system. Patients were excluded if they had an incomplete opioid prescribing history.

Frequencies of patient and prescription variables were first calculated. Then multivariate logistic regression models were constructed on the 2 primary outcomes to adjust for multiple features conjointly associated with prolonged opioid use. All of the statistical tests were 2-sided at an $\alpha$ of .05. All analyses were completed through use of R Version 3.5.1 (R Foundation for Statistical Computing).

RESULTS

Demographic features of the 9474 patients who met the inclusion criteria are listed in Table 1. The population included 1316 (14%) female and 8158 (86%) male patients. Median patient age was 27 years; however, inferential statistics were performed on 10-year age groups that spanned $\leq$20 years (756 patients; 8%), $<$30 years (5541 patients; 58.5%), $\leq$40 years (2498; 26.4%), $\leq$50 years (630 patients; 6.6%), and $>$50 years (49 patients; 0.5%). There were 4116 (43%) white patients, 1342 (14%) black patients, 259 (3%) Asian patients, 29 (0.3%) American Indian/Alaskan native patients, and 3728 (39%) patients categorized as other/unknown. We noted that 66 (0.7%) patients had a preoperative diagnosis for substance abuse (Table 1).

The most common opioid prescription was oxycodone-acetaminophen (5-325 mg), accounting for 33.5% of the total prescriptions and 34.5% of the total volume of morphine equivalents dispensed. Figures 1 and 2 depict the trend in overall opioid medications dispensed for the top prescriptions during the study period by percentage of prescriptions and total morphine equivalents, respectively.

There were 1941 (20.5%) patients who filled a prescription for opioids during the preoperative period. A total of 2656 patients (28%) continued to receive opioid prescriptions more than 90 days after surgery, and 502 patients met the definition for extreme opioid use. These 502 patients filled 73% of the total postoperative opioid prescriptions in this patient population.

When prolonged opioid use was analyzed via logistic regression, the analysis revealed significant effects of age group, sex, preoperative and perioperative opioid use, and having been diagnosed with a substance abuse disorder (Table 2). Individual parameter estimates from the regression suggested that both the younger (20-30 years of age) and older ($>$50 years of age) individuals in the cohort were at higher risk than patients aged 30 to 40 years, that women were more likely to continue to fill opioid prescriptions than men, and that race was an unimportant factor in predicting future opioid use. Patients with a history of substance abuse disorder were much more likely to fill future opioid prescriptions than those without, and that race was an unimportant factor in predicting future opioid use. Patients with a history of substance abuse disorder were much more likely to fill future opioid prescriptions than those without, and that race was an unimportant factor in predicting future opioid use.
extreme use group having been diagnosed with a substance abuse disorder. As in the analysis of prolonged opioid use, preoperative and perioperative opioid prescriptions are good predictors of extreme opioid use. For both analyses, the likelihood of a patient using postsurgical opioids decreased with each subsequent year.

### DISCUSSION

The primary finding of this study was that 28% of an otherwise healthy population comprised of more than 9000 servicemembers are actively filling opioid prescriptions at more than 90 days after surgery. Appropriate management of pain is extremely important in patient care and satisfaction, allowing for improved rehabilitation after orthopaedic injuries and procedures. However, opioid use is not without risk; excessive and inappropriate use has led to many negative consequences for patients and society.14

Patients who undergo orthopaedic surgery have elevated levels of pain with acute and chronic conditions. Postoperative management increasingly involves opioid prescriptions for pain control. One contributing factor was the American Medical Association’s recognition of pain as the “fifth vital sign” during the 1990s. Before this period, opioids were not routinely prescribed in postoperative orthopaedic care.7,17,19,21

Information regarding the percentage of patients who use opioids before surgery, the typical postoperative trends in opioid requirements, and the risk factors for prolonged opioid use after common orthopaedic procedures is necessary to help counsel patients and establish a treatment baseline for comparison while the entire orthopaedic community works to minimize prescribing opioids.4,15 Additionally, we noted an overall downward trend in the use of opioids during the observed study period. The likelihood of a patient using postsurgical opioids decreased with each subsequent year. This may be due to the attention paid to this continuing health crisis, leading to alterations in physician prescribing practices as well as patient education. However, we analyzed data from 2012 to 2015, and it is possible that the decreasing trend did not continue after this period.

Beck et al2 demonstrated a decreasing opioid demand in the immediate postoperative period after ACLR, reaching a nadir at 7 days after surgery. Overall, in each study group, those investigators noted a general decrease in narcotic use over time and increasing use of nonnarcotic agents. However, their findings were not statistically significant. Two other studies assessed opioid misuse after ACLR beyond the immediate perioperative period.1,16 Anthony et al1 performed a retrospective cohort study of a large insurance database with 4946 ACLRs performed over 8 years. The authors found that 7.2% and 4.7% of patients in their series were still filling opioid prescriptions at 90 days and 360 days postoperatively, respectively. Further, the patients younger than 25 years of age were at an elevated risk of filling opioid prescriptions postoperatively. Rao et al16 reported that 2.7% patients continued to take opioid medications between 90 and 360 days postoperatively. The

### TABLE 2
Multivariate Logistic Regression for Predictive Factors for Prolonged Opioid Use

|                      | Odds Ratio | Lower 95% | Upper 95% | P Value |
|----------------------|------------|-----------|-----------|---------|
| Sex                  |            |           |           |         |
| Female/male          | 1.21       | 1.06      | 1.38      | .004    |
| Age group, y         |            |           |           |         |
| 20/30                | 1.28       | 1.01      | 1.62      | .007    |
| 40/30                | 1.06       | 0.91      | 1.23      |         |
| 50/30                | 1.25       | 0.97      | 1.62      |         |
| ≥50/30               | 2.67       | 1.19      | 5.95      |         |
| Preoperative opioids |            |           |           |         |
| Yes/no               | 1.61       | 1.44      | 1.79      | <.0001  |
| Perioperative opioids|            |           |           | <.0001  |
| 7.5-11.2/0-7.5 mme   | 1.28       | 1.07      | 1.54      |         |
| 11.2-16.7/0-7.5 mme  | 1.59       | 1.34      | 1.89      |         |
| 16.7-18/0-7.5 mme    | 2.44       | 2.07      | 2.87      |         |
| Race                 |            |           |           | .60     |
| White/nonwhite       | 1.03       | 0.93      | 1.12      | .02     |
| Substance abuse diagnosis | 1.79 | 1.08 | 2.95 | .004 |

*mme, morphine milligram equivalents.

### TABLE 3
Multivariate Logistic Regression for Predictive Factors for Extreme Opioid Use

|                      | Odds Ratio | Lower 95% | Upper 95% | P Value |
|----------------------|------------|-----------|-----------|---------|
| Sex                  |            |           |           | .88     |
| Female/male          | 1.02       | 0.78      | 1.34      |         |
| Age group, y         |            |           |           | <.0001  |
| 20/30                | 0.69       | 0.37      | 1.31      |         |
| 40/30                | 1.31       | 0.98      | 1.76      |         |
| 50/30                | 1.98       | 1.25      | 3.13      |         |
| ≥50/30               | 2.98       | 0.68      | 13.02     |         |
| Preoperative opioids |            |           |           | <.0001  |
| Yes/no               | 2.25       | 1.85      | 2.74      |         |
| Perioperative opioids|            |           |           | <.0001  |
| 7.5-11.2/0-7.5 mme   | 1.83       | 1.12      | 2.99      |         |
| 11.2-16.7/0-7.5 mme  | 2.29       | 1.45      | 3.62      |         |
| 16.7-18/0-7.5 mme    | 7.5        | 5.03      | 11.19     |         |
| Race                 |            |           |           | .0002   |
| White/nonwhite       | 1.44       | 1.19      | 1.73      | <.0001  |
| Substance abuse diagnosis | 6.82 | 3.86 | 12.06 | .004 |

*mme, morphine milligram equivalents.

A similar logistic regression was made for predictive factors for extreme opioid use (Table 3). That analysis revealed broadly similar significant features, although sex was non-significant whereas race was significant. Perhaps unsurprisingly, when attempting to predict extreme use, we found that a substance abuse diagnosis carried a nearly 7-fold increase in risk. However, even in this population of extreme opioid users, substance abuse diagnosis was an extremely infrequent diagnosis, with only 24 (4%) in the...
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The study was unable to address patients who receive excess opioids after a procedure, which are either discarded improperly or stored in an unsecure manner, leading to potential diversion and abuse, and we are unable to document any patients returning medications in pharmacy amnesty (unused medication) boxes. Future studies comparing opioid use after elective orthopaedic procedures between military and civilian populations may elucidate factors contributing to the top 95th percentile of all opioid consumers. Despite these limitations, this study provides the largest review of opioid misuse after ACLR.

CONCLUSION

Opioid abuse is an epidemic in both civilians and military personnel. Understanding the risk factors that lead to prolonged opioid use may help guide orthopaedic surgeons as they consider how much, if any, opioid medication to provide in the perioperative and postoperative periods. Total perioperative morphine equivalents, total perioperative morphine equivalents, sex, and race were identified as potential predictors of prolonged opioid use after ACLR. This information may prove useful in developing a predictive model to identify at-risk patients before surgery as well as counseling patients to avoid prolonged use, thus allowing early intervention to prevent or mitigate future misuse.

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