

Managing Post-Operative Pain in Orthopedic Patients: An International Comparison

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ABSTRACT

Introduction. Opioids play a crucial role in post-operative pain management in America, but not in some other countries. We sought to determine if a discrepancy in opioid use between the United States (U.S.) and Romania, a country that administers opioids in a conservative fashion, would show in subjective pain control differences.

Methods. Between May 23, 2019, and November 23, 2019, 244 Romanian patients and 184 American patients underwent total hip arthroplasty or the surgical treatment of the following fractures: bimalleolar ankle, distal radius, femoral neck, intertrochanteric, and tibial-fibular. Opioid and non-opioid analgesic medication use and subjective pain scores during the first and second 24 hours after surgery were analyzed.

Results. Subjective pain scores for the first 24 hours were higher among patients in Romania compared to the U.S. ($p < 0.0001$), but Romanians reported lower pain scores than U.S. patients in the second 24-hours ($p < 0.0001$). The quantity of opioids given to U.S. patients did not differ significantly based on sex ($p = 0.4258$) or age ($p = 0.0975$). However, females reported higher pain scores than male patients following the studied procedures ($p = 0.0181$). No sex-based differences in pain scores were noted among Romanian patients.

Conclusions. Higher pain scores in American females, despite equivalent amounts of narcotics to their male counterparts, and the absence of a difference in Romanians suggested that the current American post-operative pain regimen may be tailored to the needs of male patients. In addition, it pointed to the impacts of gender, compared to sex, in pain experiences. Future research should look for the safest, most efficacious pain regimen suitable for all patients. *Kans J Med* 2023;16:56-60

INTRODUCTION

Management of post-surgical pain in the United States (U.S.) relies heavily on the use of opiates given that they are relatively inexpensive and modestly effective.¹ Furthermore, a 2020 study comparing post-operative pain management between U.S. patients and non-U.S. patients found that 91% of U.S. patients received opioids compared to 5% of non-U.S. patients.² Additionally, U.S. patients had higher opioid

refill rates at 4.7% compared to 1.0% for non-U.S. patients.

One of the major challenges in assessing pain and the impact of interventions is the subjective nature of pain reporting. While nociception (the perception of pain resulting from the neural processing of painful stimuli beginning at the nociceptors) is reliant on several inherent physiologic factors, including sex and age, the expression of pain is also dependent on social and cultural influences.³ While the physiologic factors contributing to nociception are the same across the globe, social/cultural influences may differ, resulting in differences in pain expression, the meaning of pain, assumptions about anticipated levels of pain control, and depicting uses of opioids and other pain-relieving medications and interventions.⁴

More consistent recommendations are needed to improve post-operative pain management and function while limiting the dangers of reliance on opioids. To that end, we sought to compare orthopedic post-operative pain and pain management retrospectively between patients undergoing common orthopedic procedures in the U.S. and in Romania to determine if any discrepancies in opioid use between the two countries would depict associations in pain control, including patient demographics.

METHODS

After obtaining Institutional Review Board (IRB) approval, a retrospective review of post-operative pain management was performed in orthopedic departments at a hospital in the U.S. and a hospital in Romania. Romanian data were collected in real-time for patients with the following injuries: bimalleolar ankle fractures, distal radius fractures, femoral neck fractures, hip osteoarthritis (total hip arthroplasty), intertrochanteric femur fractures, and tibial fractures with associated fibular fracture. Co-investigators (JAN and RIM) recorded for each patient the diagnosis, surgical procedure, date of operation, age, sex, presence of a spinal anesthetic block, patient-reported pain score (0-10) assessed during the first 24 hours after surgery, all analgesic medication given during the first 24 hours after surgery, patient-reported pain score (0-10) assessed between 24 and 48 hours after surgery, and all analgesic medication given between 24 and 48 hours after surgery. These data were confirmed via retrospective chart review by co-investigators (JAN and RIM). U.S. data for these injuries were collected retrospectively utilizing an informatics database, Healthcare Enterprise Repository for Ontological Narration (HERON).^{5,6} HERON is a search discovery tool that utilizes Current Procedural Terminology (CPT) and International Classification of Diseases (ICD) codes to provide researchers de-identified data from various medical center sources. The U.S. patients were identified with a HERON query utilizing CPT codes for open reduction and internal fixation (ORIF) as well as ICD codes for the following injuries: bimalleolar ankle fractures, distal radius fractures, femoral neck fractures, hip osteoarthritis (total hip arthroplasty), intertrochanteric femur fractures, and tibial fractures with associated fibular fracture.

Patients undergoing surgical treatment between May 23, 2019, and November 23, 2019, were included after review of records. Inclusion criteria included being at least 18 years of age and having documentation for patient reported pain scores at least once within 24 hours and once between 24 and 48 hours after surgery. The following patient demographics and information for each patient were recorded: age, patient

sex, diagnosis, associated surgical procedure, all analgesic medications administered in the first 24 hours after surgery (with opioid analgesics compared quantitatively using morphine milligram equivalents (MME), patient reported pain score during the first 24 hours after surgery via the previously established 0-10 Numerical Rating Scale (NRS),⁷ all analgesic medications administered between 24 and 48 hours after surgery (with opioid analgesics compared quantitatively using MME), and patient reported pain score between 24 and 48 hours after surgery. For the pain score, patients were asked to rate their pain on a 0-10 scale in which 0 represented very minimal or no pain and 10 represented the worst pain imaginable.

Post-operative care was provider-dependent. Antibiotics and deep vein thrombosis prophylaxis were prescribed as indicated by patient clinical presentation, hospital policy, and current guidelines practiced within each department. Patient follow-up was dictated by hospital policy and patient/provider preferences.

In Romania, 282 patients of 556 patients met the initial inclusion criteria for this study. After excluding 38 patients due to missing either the first or second 24-hour pain score, 244 Romanian patients were included in this study. In the U.S., there were 728 patients included in the initial results from HERON, based on patients who had undergone treatment for the defined pathologies in the established timeframe. Out of the 728 patients, 317 met the initial inclusion criteria; 131 patients were excluded because they lacked documentation of a pain score in the second 24-hour period. Accordingly, 186 American patients were included in further analysis.

Table 1 summarizes available patient demographics for the U.S. and Romanian cohorts.

There was a significant difference in the types of fractures between the countries ($p < 0.0001$): hip arthritis was more prevalent amongst patients in the U.S. as compared to Romanian patients. Romanian patients were less likely to be female than U.S. patients ($p = 0.0164$, OR = 0.6112, 95% CI[0.4149, 0.9004]). There was not a significant difference in patient age between the countries ($\Delta = 1.8925$, 95% CI[-1.3309, 5.1159], $p = 0.2491$).

Table 1. Patient demographics and injury type.

	U.S. (N = 186)	Romania (N = 244)	Total (N = 428)
Age at Injury; Mean (SD)	62.83 (16.91)	64.72 (17.41)	63.94 (17.21)
Patient Sex; Female (%)	114 (61.29%)	120 (49.18%)	234 (51.88%)
Injury Type (%)			
Hip Arthritis	99 (53.23%)	46 (17.36%)	145 (32.15%)
Intertrochanter Fracture	39 (20.97%)	94 (35.47%)	133 (29.49%)
Distal Radius Fracture	23 (12.37%)	29 (10.94%)	52 (11.53%)
Femoral Neck Fracture	4 (2.15%)	24 (9.06%)	28 (6.21%)
Bimalleolar Ankle Fracture	13 (6.99%)	37 (13.96%)	50 (11.09%)
Tibial Shaft Fracture with Fibular Fracture	8 (4.3%)	35 (13.21%)	43 (9.53%)

Categorical variables were analyzed with a chi-square test and continuous variables were analyzed with a t-test. Furthermore, the effects of the variables and their interactions on pain scores were compared via analysis of covariance (ANCOVA). A p value of less than 0.05 was considered statistically significant. Statistical analysis was performed in R [V 4.0.5].

RESULTS

A total of 180 of 186 (96.8%) U.S. patients received opioids as part of their post-operative pain management regimen, while 2 of 244 (0.82%) of Romanian patients received one dose of opioid analgesic. Pain scores for the first 24 hours were higher in Romanian patients compared to patients in the U.S. ($\Delta = 2.52$, 95% CI[2.08, 2.97], $p < 0.0001$), while pain scores were lower for the Romanian patients in the second 24 hours compared to U.S. patients ($\Delta = -1.18$, 95% CI[-1.61, -0.76], $p < 0.0001$). Furthermore, pain scores for U.S. patients increased between the first and second 24-hour periods while these scores decreased for Romanian patients (Figure 1).

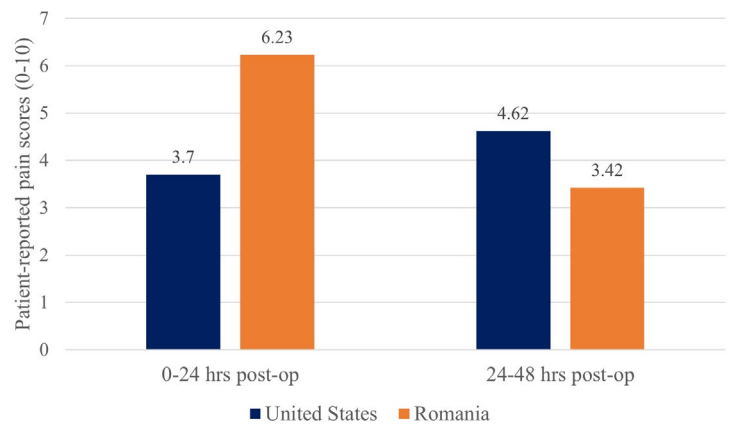


Figure 1. Post-operative pain scores from 0-10 for the 1st and 2nd 24-hour post-operative periods. Differences were statistically significant, $p < 0.05$.

In the U.S., women reported higher pain scores than men ($\Delta = -0.7211$, 95% CI[-1.3174, -0.1248], $p = 0.0181$), despite receiving statistically equal amounts of opioids ($p = 0.4258$). The effect that opioids had on a patient's pain score differed depending on surgery type ($p = 0.0215$) and were more effective at reducing pain scores after some surgeries compared to others. However, the effectiveness of opioids also did not appear to differ based on patient sex ($p = 0.4701$) or age ($p = 0.5812$). Additionally, there was no significant difference in the amount of opioid analgesic given with respect to age ($p = 0.0975$). Amongst Romanian patients, women and men did not report statistically different pain scores ($p = 0.1686$). There was no significant difference based on sex in the use of acetaminophen ($p = 0.8287$), diclofenac ($p = 0.4089$), or metamizole ($p = 0.7087$). There was also no significant difference based upon patient age for the use of acetaminophen ($p = 0.7900$), diclofenac ($p = 0.1641$), or metamizole ($p = 0.3140$).

In the U.S., the effect of acetaminophen was dependent on age ($p = 0.0372$) but not sex ($p = 0.4889$) or surgery type ($p = 0.5181$). The effect

of opioids on reported pain scores was dependent on acetaminophen dosage and vice versa ($p = 0.0034$). In Romania, the reported effect of acetaminophen did not vary based on patient age ($p = 0.5239$), and the effect of any medication (acetaminophen/diclofenac/metamizole) was not dependent on sex ($p = 0.5183/0.6586/0.7273$), surgery type ($p = 0.1587/0.7707/0.7967$) or the concurrent use of another medication. Use of diclofenac, independent of acetaminophen or metamizole, improved pain scores regardless of patient sex or age ($p = 0.0040$).

DISCUSSION

The U.S. is among the top three high-income countries for the number of opioid prescriptions per capita, with around 50,000 prescriptions per million inhabitants,⁸ while Romania provides far fewer opioid prescriptions even though it is among the top three in opioid prescribing among upper middle income countries.⁹ Although recent reports raised concern about increasing reliance on opioids in Europe leading some to question whether Europe is heading towards its own opioid crisis,^{10,11} it was clear that European opioid use was still significantly less than that found in U.S.^{8,10-13} Accordingly, the finding in this study that nearly every patient in the U.S. cohort was administered opioids was not surprising. It is unclear whether the almost exclusive reliance on non-opioid medications in Romania was due to limited access to opioids, physician preferences on pain control, or cultural or economic forces that have not made frequent opioid use a possibility. In addition, cultural influences may have impacted the patients' views of pain and options for pain control.

Our findings suggested opioid use in the first 24 hours postoperatively seemed to improve pain control. However, the Romanian non-opioid pain management regimen reported better pain control in the second 24-hour time period. Many factors likely contributed to this finding. One major contributor may be differences in managing patient expectations of post-operative pain. The evidence on the effectiveness of patient education related to pain and opioid use in reducing a patient's post-operative pain scores and/or opioid dosage was not conclusive.¹⁴ Some studies have shown specific patient education to be effective,^{15,16} while others have not shown such results.¹⁷⁻¹⁹ The results of these interventions, however, did not account for cultural differences on the meaning of pain and the pain experience consistently, making it difficult to predict results if an intervention was to be taken from one country to another,⁴ given that cultural influences related to the pain experience and expectations for pain control may be more impactful than individual education interventions.²⁰

Previous studies have compared pain and pain management outcomes across countries (Table 2). The current study contradicted results found in several of these studies which reported worse pain scores for U.S. patients in the first 24 hours despite receiving greater amounts of opioids. One possible reason for this discrepancy was that our inclusion criteria dictated patients must have a pain score in the second 24-hour period. The atypical 48-hour hospital stay suggested more complex needs and could signify more severe pain. Accordingly,

this may suggest that opioids may have a specific role in early pain management, but such a role becomes less effective with time. Additionally, many of the studies cited in Table 2 utilized the reliable International Pain Outcomes questionnaire,²¹ compared to the simple, 0-10 NRS, subjective patient reported score used in this study.

Table 2. Reported differences in pain medication administration and outcomes.

Author, year <ul style="list-style-type: none"> • <i>Study type</i> • <i>Timeframe</i> • <i>Assessment method</i> 	Differences in Pain Medication Administration and Outcomes
Chapman et al. 2013 ²² <ul style="list-style-type: none"> • International (U.S. vs. Europe) • First post-operative day • International Pain Outcomes questionnaire 	<ul style="list-style-type: none"> • 98.3% of Americans received opioids compared to only 70.2% of Europeans. • Scores were higher for Americans (7.39 ± 2.49) compared to Europeans (5.40 ± 2.74; $p < 0.0001$). • Women demonstrated higher worst pain scores compared to men ($p = 0.0007$).
Polanco-Garcia et al. 2017 ²³ <ul style="list-style-type: none"> • Single country (Spain) • Assessed at a mean of 25 hours after surgery • International Pain Outcomes questionnaire 	<ul style="list-style-type: none"> • Scores were significantly higher for patients receiving opioids (6.0 ± 2.5) compared to patients receiving multimodal pain analgesia (NSAIDs + opioids; 5.7 ± 2.5; $p < 0.05$).
Wang et al. 2021 ²⁴ <ul style="list-style-type: none"> • International (U.S. vs. China) • First post-operative day • The American Pain Society Patient Outcome Questionnaire-Revised 	<ul style="list-style-type: none"> • The most frequently prescribed type of medication was strong opioids (45.2%) in the United States compared to NSAIDs (51.1%) in China. • 54.5% of Chinese patients reported not using any analgesic method after surgery while only one American patient (0.4%) reported no analgesic use. • Pain was more severe amongst U.S. patients (23.14 ± 11.58) compared to Chinese patients (17.47 ± 10.45; $p < 0.001$).
Zaslansky et al. 2018 ²⁵ <ul style="list-style-type: none"> • International (U.S. vs. 13 countries) • First post-operative day • International Pain Outcomes questionnaire 	<ul style="list-style-type: none"> • 98.4% of Americans received opioids compared to only 71.2%, internationally ($p < 0.0001$). • U.S. patients (7.5 ± 2.5) reported higher subjective pain scores compared to international patients (5.6 ± 2.8; $p < 0.0001$).
Schnabel et al. 2020 ²⁶ <ul style="list-style-type: none"> • International (PAIN OUT Registry) • First post-operative day • International Pain Outcomes questionnaire 	<ul style="list-style-type: none"> • Females (OR = 1.433; $p < 0.001$) and younger age (OR = 1.277; $p < 0.001$) were found to be risk factors for patients of experiencing severe post-operative pain.
Borys et al. 2018 ²⁷ <ul style="list-style-type: none"> • Single country (Poland) • First post-operative day • Visual-analogue scale 	<ul style="list-style-type: none"> • Women (31 [29-33]) experienced more intense pain than men (28 [26-30]; $p = 0.044$). • Older patients (21 [18-24]) experienced less intense pain than younger patients (29 [26-33]; $p = 0.0031$) and middle-aged patients (30 [26-33]; $p = 0.0022$).

Note: NSAIDs: non-steroidal anti-inflammatory drugs

The potential influence of culture on the pain experience was noted in the gender-based differences in pain scores. Women and men received equivalent types and dosages of medications in each country, yet women in the U.S. reported higher pain scores than men, a finding that was not seen in the Romanian cohort. While the explanation of sex-based differences in pain was not completely clear, there appeared to be sex-based differences in nociception at the spinal cord and brain level.²⁸ These may be impacted further by the presence of co-morbidities, such as depression and post-traumatic stress disorder, as well as potential sex-based differences in response to opioids.²⁹

These physiologic differences may be impacted by gender-based differences in the reporting of pain, including how patients cope with pain and stereotypical gender roles. As sex-based physiologic differences in the perception of pain would exist in both countries, the differences between Romania and the U.S. in gender-based expression and reporting of pain may reflect social/cultural and stereotype differences.³⁰ This highlighted an important cultural component of pain management and may indicate not only the relative impacts of sex- vs. gender-based influences on reported pain but also the roles of improved patient and public education regarding pain and pain management. It is reasonable to suggest that cultural variances between the U.S. and Romania related to these entities of cultural/societal expectations regarding pain and pain management may explain the discrepancy found in our study.

For both U.S. and Romanian patients, neither the effect of opioids nor non-opioid analgesics was dependent on sex. These results related to opioids are contradictory to current literature that indicated that opioids may be less effective in women³¹ potentially due to the lower density of mu-opioid receptors in women compared to men.^{32,33} This relative lack of efficacy may contribute to women seeking additional opioids. A large database study in the U.S. between 2008 and 2018 found opioid prescription fill rates were disproportionately higher among men and women aged ≥ 65 years and women of all ages.³⁴ However, other factors need to be explored to understand these prescribing tendencies, as well as why in our study women reported higher pain scores than men, despite receiving statistically equal amounts of opioids and that there were no differences with respect to sex in the effectiveness of opioids at reducing pain scores. Higher rates of opioid prescription and use in women compared to men have been documented,³⁵ which perhaps exists as a surrogate for poor understanding of pain and opioid response in this population.

Lastly, the findings of this study highlighted the role for multi-agent, non-opioid analgesia in post-operative pain management. Martinez et al.³⁶ noted that concurrent use of non-steroidal anti-inflammatory drugs with opioids can lead to a reduction of opioid use by up to 50%, while diclofenac was associated with opioid reductions of 17%-50%. However, differences between women and men in these responses need to be evaluated. Better understanding is needed of the factors that contribute to the pain experience in order to decrease the use of opioids, while improving patient outcome and function.

Limitations. The following limitations were noted. Assessment of peripheral nerve blocks or other types of regional anesthesia in either country that may have contributed to differences in pain scores was not conducted. Due to the differences in the non-opioid analgesics used

between countries and due to the lack of standardization or homology amongst non-opioid analgesics in general, it was not possible to quantitatively compare the non-opioid analgesics administered between each country or between injury pathologies. To provide accurate comparison of patient reported pain outcomes, patients were excluded if they lacked documentation for a pain score between 24 and 48 hours after surgery. Accordingly, the patients included in our study may have had more extensive injuries or complicated surgeries leading to relatively more pain and/or the possibility for complications compared to patients who would have been discharged before 24 hours after surgery. Finally, given the retrospective nature of this study, data were reliant upon proper documentation and charting.

CONCLUSIONS

For the presented study, opioid use in the first 24 hours after surgery showed improved pain control, but this was not seen in the following 24 hours. In the U.S., women reported higher pain than men, despite being given statistically equivalent amounts of opioids, yet in Romania, pain scores from men and women were not statistically different. This finding suggested possible cultural differences between the U.S. and Romania as it related to expectations of pain and pain control, especially for women patients, and that pain management protocols in the U.S. may be tailored more to the needs of men. Pain management is a complex process involving many factors (e.g., medication, sex, gender, age, race, and culture), and further research needs to be performed to determine the safest, most efficacious interventions to improve the function of individual patients.

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