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Opioid-free shoulder arthroplasty: a prospective study of a novel clinical care pathway

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Background: Opioid therapy has been a cornerstone of perioperative pain control for decades in the United States, despite our increased understanding of the morbidity and mortality linked to opioids. The purpose of this study is to explore the safety, efficacy, and feasibility of an entirely opioid-free perioperative pathway in patients undergoing elective shoulder arthroplasty.

Methods: Thirty-five patients undergoing elective total shoulder arthroplasty with a mean age of 71 (range, 50-87) years elected into a comprehensive opioid-free, multimodal pain management protocol. Opioid use was completely eliminated for all points in the perioperative period including during regional and general anesthesia. Data were collected regarding patient-reported pain, opioid consumption in the perioperative period, postoperative delirium, nausea, constipation, and falls.

Results: Pain level at the primary outcome point of 24 hours or discharge was rated at 2.5 on the numeric rating scale. Stable, low pain scores were demonstrated at all time points postoperatively. Low rates of nausea, falls, and constipation were reported. Only 1 patient required ''rescue'' opioid medications during the in-patient stay, and an additional patient was given a low-dose opioid prescription at the 2-week postoperative appointment.

Conclusions: An opioid-free, multimodal pain management pathway is a safe and effective option in properly selected patients undergoing shoulder arthroplasty with a very low risk of requiring rescue opioids. This study is the first such study to present a surgical protocol entirely free of opioids at all portions of the patient care pathway.

Level of evidence: Level IV; Case Series; Treatment Study

Keywords: Arthroplasty; pain; multimodal; shoulder; opioid; opioid-free

Opioid-based analgesia has been a cornerstone of patient care in the setting of acute pain for the last century and has undergone logarithmic increase over the past 20 years. This rise in its use has prompted a rise in opioid-induced side effects. These include constipation, nausea/vomiting, hyperalgesia, delirium, and several others (urinary retention, withdrawal symptoms, depression,

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This study received IRB approval from Advarra Center for IRB Intelligence (Pro00021833).

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Table I Inclusion and exclusion criteria

Study criteria	
Inclusion	Exclusion
Patients were included if they had a treatment of any of the following: • Osteoarthritis • Avascular necrosis • Cuff tear arthropathy • Inflammatory arthritis etiologies	Patients were excluded if they had any of the following: • Revision total shoulder arthroplasty • Chronic opioid therapy • Liver or renal insufficiency • Arthroplasty for fracture • Sickle cell compensation • Chronic anticoagulation therapy • Workers compensation • Inability to receive block

respiratory depression, and death).[14,18,25,27,31,36,47] Patient expectations of opioid-based pain medication have driven a rapid rise in outpatient opioid prescriptions including both short- and long-acting opioids.[27] These prescriptions have in turn become a source of significant mortality in the United States, with nearly 20,000 deaths due to prescription opioid overdose in 2014 alone. The Center for Disease Control and Prevention revealed that 6% of all-cause patients discharged with at least 1 day of opioid therapy were still on opioids at 1 year. That number grew to 13.5% after 8 days of opioid use.[41] Long-term preoperative opioid use has also been correlated with inferior clinical outcomes for many orthopedic procedures.[13,22,34,37,39,42,45]

There have been momentous efforts made in identifying synergistic compounds to use for acute pain management in the perioperative period to minimize opioid requirements. These studies have focused on neuromodulation with gabapentinoids,[10,32,40] intravenous and local administration of sodium-channel blockers such as lidocaine and bupivacaine,[4,29,43] and in nonsteroidal anti-inflammatories and acetaminophen.[20,21,23,35,38] Although studies have extensively evaluated multimodal treatments for opioid reduction, no study has looked at the possibility of using a comprehensive perioperative pain control pathway that entirely removed opioid medications.

Arthroplasty continues to be a dominant procedure and accounts for well over a million surgeries performed in the United States per year. With the ability to use targeted nerve blocks,[2,5,46] and the increasing data showing efficacy of multimodal therapy for acute pain,[1,7,12,15,16,30] we propose a patient care pathway that is free of all opioid-based medications. From the time that patients are checked in until clinic follow-up, they will use a pathway designed to properly manage pain and eliminate opioid-related side effects after shoulder arthroplasty. Therefore, the purpose of this study is to investigate the safety, efficacy, and feasibility of an opioid-free perioperative pathway in patients undergoing elective shoulder arthroplasty.

Materials and methods

After institutional review board approval, patients were approached to participate in this nonrandomized clinical trial. Patients, aged 50 or older, undergoing elective primary total shoulder or reverse total shoulder arthroplasty agreed to voluntarily participate in this study as a part of an opioid-free pain-management pathway. Before enrolling a patient in the study, the research team reviewed all inclusion and exclusion criteria as outlined in Table I. Patients in the study group had to be able to receive nonsteroidal anti-inflammatory medications (NSAIDs); thus, creatinine clearance less than 30 mL/min or allergies to NSAIDs were additional exclusion criteria for participation in the study.

Pain management protocol (Table II)

In the preoperative area, patients in the study received an oral dose of both gabapentin and celecoxib. In the event of sulfa allergy, a patient received an oral dose of meloxicam in lieu of celecoxib. In addition, an ultrasound-guided, single-shot interscalene block was placed preoperatively by a board-certified anesthesiologist without opioid comedication. Intraoperative management by the anesthesia team was performed with nonopioid modalities. All interventional patients received intravenous acetaminophen during the procedure. Anesthetic modalities included, but were not limited to, regional block, propofol, IV lidocaine, rocuronium/vecuronium, and sevoflurane/desflurane. Liposomal bupivacaine (20 cc) suspended in bupivacaine (0.25%, 20 cc) was injected into the periarticular soft tissues, as previously described, as an adjunct to the block performed by the anesthesia team.[3]

After the procedure, patients received scheduled high-volume cryotherapy, gabapentin (300 mg q8hr), and ketorolac (15 mg IV q6hr for 4 doses). Ketorolac was transitioned to celecoxib (or meloxicam for patients with sulfa allergy) for the duration of the hospitalization. Pro re nata (PRN) medications included both oral and intravenous acetaminophen, as well as an additional 15 mg of ketorolac per 6-hour period. Patients with creatinine clearance between 30 and 60 mL/min received a half-dose of all NSAIDs.

In addition, the nursing staff was instructed to notify the physician team if the patient reported pain that was inadequately controlled under the interventional pathway, including the PRN medications. After exhausting all nonopioid modalities, the

Table II Pain management protocol outline

Stage	Therapies
Preoperative	• Gabapentin 300 mg PO × 1 • Celecoxib 200 mg PO × 1 • Intrascalene block
Intraoperative	• Acetaminophen 1000 mg IV × 1 • Periarticular injection: liposomal bupivacaine (20 cc) and 0.25% bupivicaine (20 cc) • Nonopioid anesthetics (fluranes, propofol, etc.)
PACU	• Ketorolac 15 mg IV × 1 • Initiation of cryotherapy
Postoperative/ floor	• Maintenance of cryotherapy • Ketorolac 15 mg q8hr × 5 doses • Celecoxib 200 mg q day after ketorolac • Gabapentin 300 mg q8hr • Acetaminophen 500 mg PO q6 PRN pain • Acetaminophen 1000 mg IV q6 PRN pain
Discharge	• Gabapentin 300 mg q8hr × 14 days • Celecoxib 200 mg q day × 14 days • Acetaminophen 500 mg q4hr PRN

PACU, post-anesthesia care unit; *PRN*, pro re nata.

administration of an opioid would be approved for patients with poorly controlled pain. On discharge, patients continued gabapentin 300 mg q8hr for an additional 14 days, as well as celecoxib (or meloxicam for those with sulfa allergies) for an additional 14 days. Patients were also allowed to continue acetaminophen as needed. No opioid prescriptions were given at the time of discharge or at follow-up.

Outcomes measures

Pain levels for all patients were assessed with a numeric rating scale in the perioperative period. Patients were also given a diary to record their pain levels postdischarge. Patient-reported numeric rating scale scores were recorded preoperatively and then at predesignated intervals through discharge. After discharge, patients were asked to record their pain at 8-hour intervals for the first 3 days after discharge. After the third day, patients were asked to record their pain daily until their 2-week follow-up appointment. Because of varying times between surgery and hospital discharge, patient pain is reported as hours postsurgery. Time was then categorized into the predesignated intervals during hospital stay followed by 8-hour intervals for 4 days and then 1-day intervals for the remainder of the study. Patients who had multiple pain records within a single time category were averaged and reported in the results. In addition, opioid consumption was recorded during hospitalization.

Opioid-related side effects including constipation, delirium, falls, and nausea were also recorded. Delirium was quantified in a binary fashion using the validated Confusion Assessment Method for nurses.[17] In addition to the patient-reported pain scores, patients were asked to complete 3 patient-reported outcome measures at the preoperative, 2-week, and 2-month visits: American Shoulder and Elbow Surgeons questionnaire, Simple Shoulder Test, and the Veterans RAND 12-item health survey.

Standard descriptive statistics are reported including frequency, measure of central tendency, and variation. All statistical analyses were carried out in SAS version 9.4 (SAS, Cary, NC, USA).

Results

Patient demographics

All 35 patients were enrolled in the study and completed surgery and follow-up. The median age of participants was 70.8 years. Females made up 51.4% of the study. A total of 54.3% of patients received a reverse total shoulder arthroplasty (TSA) (N = 19) and 16 patients received an anatomic shoulder arthroplasty (Table III).

Pain

At baseline, patient-reported visual analog scale pain scores showed a median of 6 (interquartile range: 4-8). By 6 hours postoperatively, patients reported a median pain score of 0 (0-0), and by 12 hours postoperatively, patients continued to report a median pain score of 0 (0-3). At discharge, median patient-reported pain was 2 (0-5). Pain was reportedly highest 32 hours postoperatively with a median of 4 (1-5) and leveled out consistently under a median of 3 after 3 days postoperatively. Raw patient-reported visual analog scale pain scores over time from baseline to 7 days postoperatively with a trend line connecting median pain scores for each time category are shown in Figure 1.

Rescue medications and opioid usage

Each patient received 300 mg of perioperative gabapentin, 400 mg of perioperative celecoxib, 1000 mg of intraoperative IV acetaminophen, and 266 mg of intraoperative liposomal bupivacaine. Of the 35 patients, 26 (74.3%) received at least 1 postoperative dose of acetaminophen. The median dose of 1000 mg (range: 500-1650 mg) of acetaminophen was administered to 19 of those patients. No patient required a third dose of acetaminophen. Two patients received opioids in the postoperative period. One patient had a failed interscalene block and had 1 dose of an intravenous opioid while in post-anesthesia care unit (PACU) and 2 oral doses of oxycodone during their hospitalization. They did not require an opioid prescription at discharge. During hospitalization, these 3 doses accounted for a total opioid dose of just 12 morphine milligram equivalents. One patient requested a prescription at their 2-week follow-up to address anxiety surrounding pain, but utilization data were unavailable. There were no other cases of patients requesting stronger medications after hospital discharge.

Table III Patient demographics

Covariate	N = 35
Sex, n (%)	18 (51.4)
Female	
Male	17 (48.6)
Tobacco use, n (%)	13 (37.1)
Former	
Never	22 (62.9)
Preop opioid use, n (%)	33 (94.3)
No	
Yes	2 (5.7)
Depression, n (%)	
No	34 (97.1)
Yes	1 (2.9)
Age (yr), median (IQR)	72.5 (66.3, 78.4)
BMI, median (IQR)	29.3 (25.4, 33.7)
CCI, median (IQR)	0 (0, 0)

IQR, interquartile range; *BMI*, body mass index; *CCI*, Charlson Comorbidity Index.

Patient-reported outcomes

There were no reports of delirium or falls in the hospital. There were no cases of gastritis or acute renal failure. At the 2-week follow-up visit, 37.1% (N = 13) of patients reported symptoms of constipation. Five patients (14.3%) reported having fallen at 2 weeks and only 1 patient reported having experienced nausea at 2 weeks. Results of patient-reported outcomes are outlined in Table IV at preoperative, 2-week, and 2-month follow-up visits. Of 35 patients, 34 were satisfied with pain levels and pain control regimen at the 2-week follow-up assessment.

Discussion

Abuse and addiction from opioids continues to be a large individual and societal burden in the United States. With the rising rate of deaths from opioid-specific overdoses, both prescribed and not, the medical community is rightfully looking at ways to minimize opioid use in patient care pathways. Longer-term studies are showing that even short prescriptions for acute conditions can snowball into prolonged opioid use. The Centers for Disease Control and Prevention (CDC) recently highlighted these trends, showing that patients prescribed as few as 1 day of opioids had a 6% chance of still using opioids at 1 year, and those prescribed 8 days of therapy had a 13.5% chance of continued therapy at 1 year.[41] Even more striking were the data provided by Martin et al that showed that 50% of patients who were started on a long-term opioid therapy for 90 days were still using opioids in a chronic fashion at 5 years.[30] One limitation, however, of the preceding 2 studies is their large database nature. The study populations were not controlled for etiology, type, or volume of opioid therapy, the exception being the 90-day requirement for the Martin study.

Recently, many states have begun to enact prescribing laws for opioid-based medications. These primarily limit the length of prescriptions that can be provided at an initial encounter (typically around 5 days) as well as requiring prescribers to use their state's controlled substance reporting system for each prescription.

Aside from abuse and addictive potential, opioid medications have also been shown to have deleterious side effects. Well-known opioid-related side effects include constipation, bladder dysfunction, delirium, respiratory depression, depression, and fall risk.[14,18,25,27,36,47]

These pervading issues prompted our study team to ask the question as to whether we would be able to remove opioid medications from our entire care pathway. Many studies to date have looked at the opioid-sparing impact of multimodal treatments, with both pharmacologic and nonpharmacologic interventions.[2,4-7,9-12,15,16,18-21,23,24,26,28-30,32,35,38,40,44,48,49] No study to date has explored the possibility of removing opioids entirely from the entire course of care. Our study is unique in that patients were not provided access to opioids as a part of their care pathway at any point, including their posthospitalization period. By not providing patients an opioid prescription at discharge, we are eliminating the home stores of unused opioid-based medications. Previous studies have shown that 75% of opioid overdoses seen in the emergency department are from nonprescribed or diverted opioid medications, rather than their own prescribed opioids.[8] By eliminating extraneous physical opioid tablets, they will no longer be available for abuse, misuse, and diversion in the future.

Functionally, our protocol was designed to target multiple modalities for patient comfort at all care points in the perioperative period. Preoperative dosing of gabapentanoids and nonsteroidal anti-inflammatories has become an interesting focus in recent literature, with current systematic reviews and metaanalyses in spine and arthroplasty surgeries showing a reduction in pain and opioid consumption postoperatively.[6,7,10–12,19,24,26,28,32,40,48] We additionally used liposomal bupivacaine as an adjunct to the single-shot interscalene block where we have anecdotally seen an improvement in ''rebound pain'' after the block wears off. There have been recent data that call into question the efficacy and cost-effectiveness of liposomal bupivacaine.[33] There are alternative local anesthetic compounds that may be used as an alternative to liposomal bupivacaine that may also help with rebound pain.[8]

Pre- and postoperative ketorolac and celecoxib (after the 24-hour mark) allow us to target inflammation in a methodical fashion, with more and more research supporting preoperative dosing in addition to the known benefits of anti-inflammatories postoperatively. Acetaminophen also, in both oral and intravenous form, has received renewed interest in efficacy, particularly with studies

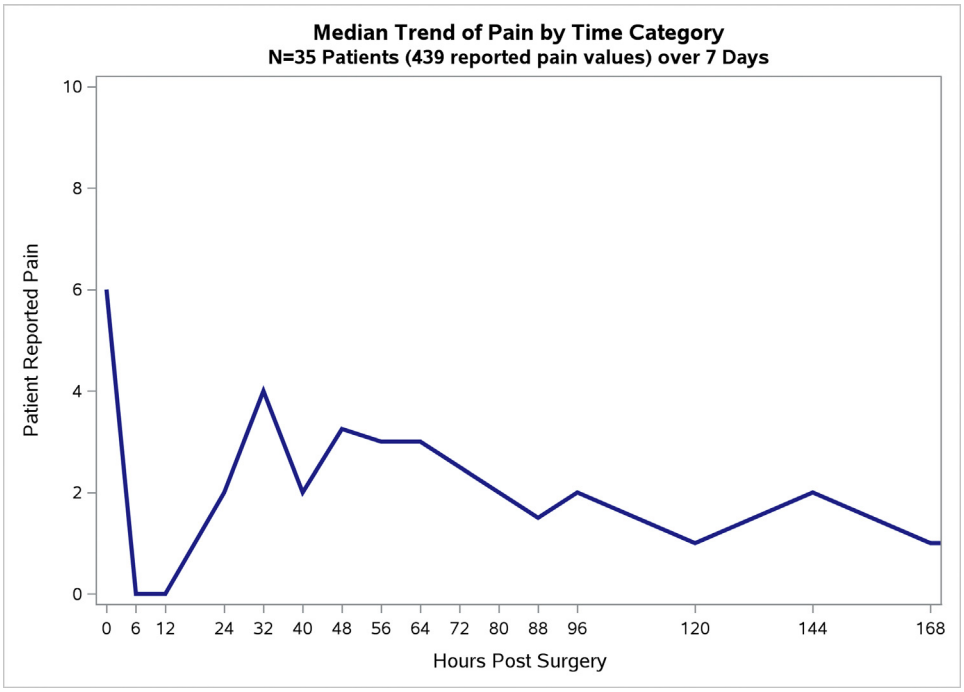

Figure 1 Median trend of patient-reported pain by time categories.

Table IV Patient reported secondary outcomes stratified by event time

Patient-reported outcomes	Stratified by event time		
	Preop*	2-week visit	2-mo visit
Constipation, N (%)	–	13 (37.1)	4 (12.9)
Nausea, N (%)	–	1 (2.9)	1 (3.1)
Fall, N (%)	–	5 (14.3)	4 (12.9)
Pain satisfaction, N (%)			
Satisfied	–	34 (97.1)	29 (93.5)
Unsatisfied	–	1 (2.9)	2 (6.5)
ASES ADL, median (IQR)	13.0 (9.0, 16.0)	5.0 (2.0, 9.0)	14.0 (11.0, 19.0)
ASES function, median (IQR)	52.5 (43.3, 65.0)	54.2 (46.7, 60.0)	71.6 (63.8, 78.3)
VR-12 PC, median (IQR)	37.4 (33.9, 42.4)	35.0 (29.1, 43.7)	40.3 (33.8, 47.0)
VR-12 MC, median (IQR)	59.4 (51.7, 62.7)	59.1 (52.5, 64.1)	60.8 (49.4, 64.0)
SST, median (IQR)	5.0 (3.0, 6.0)	2.0 (1.0, 4.0)	6.0 (4.0, 7.0)

ASES, American Shoulder and Elbow Surgeons; *ADL*, activities of daily living; *IQR*, interquartile range; *VR-12 PC*, Veterans RAND 12-item Physical Component; *VR-12 MC*, Veterans RAND 12-item Mental Component; *SST*, Simple Shoulder Test.

* Constipation, nausea, fall, and pain satisfaction were not collected preoperatively.

showing a combined effect with nonsteroidal anti-inflammatories in reducing postoperative pain, minimizing adverse events, and minimizing opioid-based analgesia.[7,9,12,15,16,20,21,23,24,30,31,48]

Our opioid-free clinical pathway also included communication and education with the patients and nursing staff regarding pain and available analgesic modalities. We invested time in educational sessions for the perioperative and floor nursing staff emphasizing the value of non-pharmacological modalities including cryotherapy as well as the benefit of nonopioid medication options.

There are several limitations to this study. First, enrollment into the opioid-free clinical pathway was done on a voluntary basis if a patient met inclusion criteria. Patients who were interested in trying a new opioid-free treatment pathway by definition are displaying an increased level of resilience and dedication to the concept being tested. Although a randomized comparison to a control would have been beneficial for clarity in the data, we again felt it important to pilot this protocol in a nonrandomized fashion, as there is no precedent in the literature for this pathway. This study allows important preliminary data to

base a larger-scale randomized trial. Secondly, patient-kept diaries continue to be a difficult data point on which to rely. Exact timing of pain score recording and recall bias introduced into the data recording can cause some aberration from investigator-collected data points. Thirdly, this study only examines the short-term recovery of the patients undergoing shoulder arthroplasty and does not allow for long-term clinical assessment. Finally, we did not assess cost of the care pathway in this study. As mentioned previously, the use of liposomal bupivacaine or intravenous acetaminophen may be an unnecessary cost when compared with related treatments that may have similar efficacy.[50] As this was a pilot study without a control group, we elected to proceed with an exploration of viability as a pathway with future studies to evaluate and potentially improve on cost metrics.

Conclusion

An opioid-free, multimodal pain management pathway is a safe and effective option in properly selected patients undergoing shoulder arthroplasty with a very low risk of requiring rescue opioids. Further investigation is needed to determine the applicability of this protocol in a more generalized population.

Disclaimer

Patrick M. Connor has received consultant payments from Lima as well as from Biomet, and also received IP royalties from Zimmer.

Shadley C. Schiffern received consultant payments from Lima USA and Wright Medical Technology, Inc.

Donald F. D'Alessandro received royalties and consultant payments from Zimmer Biomet where he was also a paid presenter/speaker.

Nady Hamid received consultant payments from Biomet.

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