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Can We Eliminate Opioids After Anterior Cruciate Ligament Reconstruction?

A Prospective, Randomized Controlled Trial

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Background: Multimodal pain protocols have been effective for postsurgical pain control; however, no published protocol has been effective in eliminating opioid consumption.

Purpose: To compare a multimodal nonopioid pain protocol versus traditional opioid medication for postoperative pain control in patients undergoing anterior cruciate ligament reconstruction (ACLR).

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: A total of 90 patients undergoing primary ACLR were assessed for participation. We performed a prospective, randomized controlled trial in accordance with the CONSORT (Consolidated Standards of Reporting Trials) 2010 statement. The study arms were a multimodal nonopioid analgesic protocol (acetaminophen, ketorolac, diazepam, gabapentin, and meloxicam) and a standard opioid regimen (hydrocodone-acetaminophen), and the primary outcome was postoperative visual analog scale (VAS) pain scores for 10 days. Secondary outcomes included patient-reported outcomes, complications, and satisfaction. The observers were blinded, and the patients were not blinded to the intervention.

Results: A total of 9 patients did not meet inclusion criteria, and 19 patients declined participation. Thus, 62 patients were analyzed, with 28 patients randomized to the opioid group and 34 to the multimodal nonopioid group. Patients receiving the multimodal nonopioid pain regimen demonstrated significantly lower VAS scores compared with patients who received opioid pain medication ($P < .05$). Patients were administered the Patient-Reported Outcomes Measurement and Information System Pain Interference Short Form, and no significant difference was found in patients' preoperative scores (opioid group, 58.6 ± 7.9; multimodal nonopioid group, 57.5 ± 7.4; $P = .385$) and 1-week postoperative scores (opioid group, 66.3 ± 8.2; multimodal nonopioid group, 61.4 ± 8.8; $P = .147$). When we adjusted for possible confounders (age, sex, body mass index, graft type), no significant differences in pain control were found between the 2 groups. The most common adverse effects for both groups were drowsiness and constipation, with no difference between the groups. All patients in the multimodal nonopioid group reported satisfactory pain management.

Conclusions: A multimodal nonopioid pain protocol provided at least equivalent pain control compared with traditional opioid analgesics in patients undergoing ACLR. Minimal side effects, which did not differ between groups, were noted, and all patients reported satisfaction with their pain management.

Keywords: knee ligaments; ACL; NSAIDs; pain control, opioids

Postoperative pain management remains one of the most challenging aspects of patient care. Opioid prescriptions in the United States increased from 76 million in 1990 to a peak of 255 million in 2012, with a 6-fold increase in opioid-associated deaths between 1990 and 2017.[1,5] Studies have shown that approximately 75% of patients seeking treatment for opioid addiction were introduced to opioids via narcotic pain medication.[6,9]

Orthopaedic and spine conditions combined account for a large percentage (27.7%) of opioid prescriptions in the United States.[24] Surgeons find themselves in the precarious position of wanting to minimize opioid use and optimize postoperative pain control and patient satisfaction.[12,13,15] Anterior cruciate ligament reconstruction (ACLR) was estimated to have increased by 67.8% nationally between 1997 and 2006.[17] Because postoperative opioids are traditionally prescribed after ACLR, the surgery presents a potential target for the reduction of narcotic prescriptions.

Apart from opioids, a variety of pain control strategies are used by orthopaedic surgeons and anesthesiologists when addressing postoperative pain. In addition to ice

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and compression, other options include pain relievers (eg, acetaminophen), nonsteroidal anti-inflammatory drugs (eg, ibuprofen, meloxicam), neuropathic pain medications (eg, gabapentin, pregabalin), antispasmodics (eg, methocarbamol, tizanidine, diazepam), and even local or regional anesthetics (eg, lidocaine, bupivacaine). Multimodal analgesia aims to combine these options for a multifaceted therapeutic approach. Multimodal analgesia is effective in decreasing postoperative opioid burden after ACLR.[2,7,18] More recently, a novel, multimodal, nonopioid pain regimen was suggested to provide adequate pain control after common sports procedures.[19] However, completely eliminating opioid use after ACLR has proved to be challenging with previous protocols.

The purpose of this study was to perform a randomized controlled trial (RCT) comparing a multimodal nonopioid pain protocol versus traditional opioid medication for immediate postoperative pain control as assessed via the Patient-Reported Outcomes Measurement and Information System Pain Interference Short Form (PROMIS PI-SF) and a visual analog scale (VAS) in patients undergoing ACLR. Secondary objectives were to compare frequency and duration of adverse events between treatment groups. We hypothesized that a multimodal nonopioid protocol would lead to no significant difference in postoperative pain control compared with a standard opioid regimen.

METHODS

Study Design

This study was designed as a prospective RCT in accordance with the CONSORT (Consolidated Standards of Reporting Trials) statement.[25] The hypothesis was formulated before collection of data. The study was reviewed and approved by our institutional review board (IRB No. 12315) and was registered at ClinicalTrials.gov (NCT03818932).

Between February 2019 and January 2020, a total of 90 patients undergoing primary ACLR by 2 fellowship-trained sports surgeons at a single academic center were screened for study eligibility (V.M., K.R.O.). Ultimately, 62 patients with a torn ACL consented to participate. The inclusion criteria consisted of patients aged >14 years and patients undergoing primary ACLR. Patients were excluded if they had a history of opioid abuse documented in the medical record, recent or current pregnancy, contraindication to the use of nonsteroidal anti-inflammatory drugs (NSAIDs) (eg, renal impairment, peptic ulcer disease, gastrointestinal bleeding), intolerance or allergy to any of the component medications, or history of same-joint surgery for any reason in the previous year or if they were undergoing revision surgery. All concomitant meniscal and cartilage procedures were recorded.

Randomization and Masking

Patients who consented to participate were randomly assigned preoperatively to either an opioid or a multimodal nonopioid pain regimen with a 1:1 allocation ratio using adaptive randomization computer software (Adaptive Randomization; MD Anderson Cancer Center). Patients declined to participate for a number of reasons including reluctance to participate in a research study and inability or lack of interest in maintaining compliance with study protocol. At 1 week before surgical intervention, surgeons were notified by secure email of the patient's group designation.

Interventions

Patients underwent an arthroscopically assisted ACLR using bone-patellar tendon-bone autograft or hamstring autograft via anatomic femoral and tibial tunnels. The patients individually determined their graft choice after an informed discussion on potential options with their surgeon. Within 2 hours preoperatively, both groups received 1-time doses of 400 mg of celecoxib orally, 975 mg of acetaminophen orally, 300 mg of gabapentin orally, 8 mg of dexamethasone intravenously, and 50 mg of tramadol orally. All ACLRs were performed with the patient under preoperative blocks at the discretion of the anesthesiologist (4 femoral nerve blocks, 58 adductor canal nerve blocks).

Intraoperatively, a local infiltration cocktail was injected evenly in 2-mL increments along the incision and the subcutaneous tissues before wound closure using a 20-mL syringe with a 1-inch, 22-gauge needle. The local infiltration cocktail consisted of the following: 150 mg (30 mL) of 0.50% ropivacaine, 30 mg (1 mL) of ketorolac, and 1 mg (1 mL) of epinephrine.[22]

Patients in the multimodal nonopioid group received a novel nonopioid multimodal analgesic protocol previously described.[19] Acetaminophen and NSAIDs (ketorolac and meloxicam) were used to target the pain cascade and postoperative inflammation, respectively. Gabapentin was used to address neuropathic pain and diazepam to control muscle cramps and spasm. Medication dosage and frequency are described in Table 1. It must be noted that patients in the multimodal nonopioid group received 1

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TABLE 1
Multimodal Nonopioid Pain Regimen[a]

Postoperative Days 1-5			
Morning	Noon	Afternoon	Evening
• Ketorolac, 10 mg	• Ketorolac, 10 mg	• Ketorolac, 10 mg	• Ketorolac, 10 mg
• Gabapentin, 300 mg	• Gabapentin, 300 mg	• Gabapentin, 300 mg	• Diazepam, 5 mg
• Diazepam, 5 mg	• Diazepam, 5 mg	• Diazepam, 5 mg	
• Acetaminophen, 1000 mg	• Acetaminophen, 1000 mg	• Acetaminophen, 1000 mg	
Postoperative Days 6-14			
Morning	Afternoon	Evening	
• Meloxicam, 7.5 mg	• Meloxicam, 7.5 mg	• Diazepam, 5 mg	
• Diazepam, 5 mg	• Diazepam, 5 mg	• Acetaminophen, 1000 mg	
• Acetaminophen, 1000 mg	• Acetaminophen, 1000 mg		

[a]Preoperative regimen (administered within 2 hours of surgery): 400 mg of celecoxib, 975 mg of acetaminophen, 300 mg of gabapentin, and 50 mg of tramadol administered orally and 8 mg of dexamethasone administered intravenously. Intraoperative local infiltration analgesia: 150 mg (30 mL) of ropivacaine, 30 mg (1 mL) of ketorolac, and 1 mg (1 mL) of epinephrine. Gabapentin weaning began on postoperative day 6 in the following manner: 400 mg in the morning and 400 mg in the evening on days 6 and 7, 400 mg in the morning on days 8 and 9, and discontinuation on day 10.

dose of 50 mg (5 morphine milligram equivalents [MME]) of tramadol before surgery.

Patients enlisted in the opioid group were prescribed 40 pills, each containing 5 mg of hydrocodone and 325 mg of acetaminophen, and were instructed to take 1 or 2 pills orally every 4 to 6 hours as needed for moderate to severe postoperative pain. This was the standard of care at the authors' institution, and patients in the opioid arm received no other pain medications.

Patients were discharged home on the day of surgery per their group designation pain protocol. All patients were encouraged to contact the on-call physician if pain was unbearable or they were experiencing any complications. Patients in both groups were given instructional pamphlets on the effects of opioids, ways to effectively manage pain postoperatively, and pain treatment goals after surgery.

Outcomes

Data collection was performed by observers who were blinded to group randomization. Patients were instructed to complete the PROMIS PI-SF questionnaire preoperatively. After surgery, a mobile messaging-based software (Mosio; Mosio Inc) was used to collect patient data. Surveys were sent to patients 3 times a day for 10 days postoperatively. A 10-day follow-up was selected to evaluate pain control in the acute postoperative period when patients are typically most susceptible to surgical pain.

Patients were asked to report their current pain level 3 times per day using a VAS score (range, 0-10, where 10 = maximum). Patients were asked to report medical side effects each evening, as well as how many opioid pills were taken in the last 24 hours (if applicable). Opioid consumption was converted to MME. At the first postoperative visit (7-10 days), patients completed the PROMIS PI-SF questionnaires.

The following variables were obtained from medical records: demographic characteristics, smoking status, anxiety/depression status, workers' compensation status, history of opioid abuse, and preoperative opioid consumption.

Statistical Analysis

The primary outcome of this study was an average daily pain difference of 1.3 points on the VAS score, as a previous study has demonstrated that this difference represents the minimal clinically important difference for the VAS pain score.[8] Prestudy power analysis, using a power of 80% (β level = .80, α level = .05), revealed that a minimum of 25 patients per group (n = 50) would be necessary to properly evaluate the primary hypothesis. A sample size of 90 patients (45 per group) was selected to account for patients with incomplete data collection (eg, lost to follow-up). Secondary outcomes included patient-reported outcomes, demographic differences, complications, and patient satisfaction. There was no crossover of patients between study arms.

Continuous data were summarized using mean and standard deviation for normally distributed variables and median with interquartile range for nonnormally distributed variables; categorical data were reported as counts with percentages. For continuous variables, univariate 2-group comparisons were performed using independent 2-sample *t* tests when the variable was normally distributed and Wilcoxon rank sum tests when the variable was nonnormally distributed. For categorical variables, univariable 2-group comparisons were performed using the chi-square test when expected cell counts were $\geq$5 and the Fisher exact test when expected cell counts were <5. The Pearson coefficient (*r*) was used to establish correlation between outcome measures. Correlation strength was defined as very high (*r* = 0.90-1.00), high (*r* = 0.70-0.89), moderate (*r* = 0.50-0.69), and low (*r* = 0.30-0.49).[20] Repeated-measures analyses were performed using mixed models and included the effects of time and group and

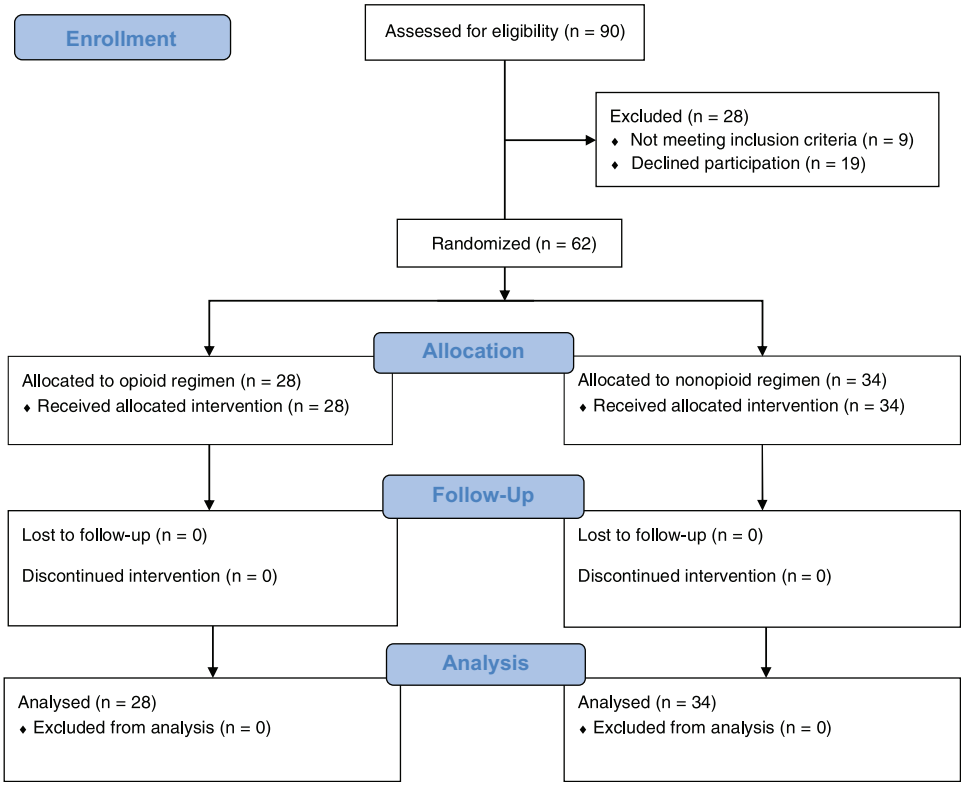

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram.

the interaction between time and group. Models were then adjusted using specified variables selected a priori in an attempt to adjust for possible confounders. Predicted means resulting from the adjusted models were plotted for the outcome variables. If needed, significant interaction effects were analyzed using post hoc comparisons using a Tukey-Kramer P value correction. Predicted means resulting from the adjusted models were plotted for the outcome variables. Statistical significance was set at $P < .05$ for group comparisons and main effect testing and $P < .10$ for interaction testing. All analyses were performed using SAS Version 9.4 (SAS Institute Inc).

RESULTS

Group Characteristics

A total of 90 consecutive patients undergoing primary ACLR were assessed for participation (Figure 1). The mean age of patients included in the analysis was 27.3 ± 12.7 years (range, 14-65 years), the mean body mass index (BMI) was 27.5 ± 4.6, and 54.8% of patients were male. Baseline characteristics and concomitant procedures are listed in Table 2. No significant demographic differences were found between the 2 groups.

Opioid vs Multimodal Nonopioid Analgesia

Patients treated with a multimodal nonopioid pain regimen demonstrated significantly lower VAS scores compared with patients who received the opioid regimen (mean difference, 1.56; 95% CI, 1.35 to 1.78; $P < .001$) (Figure 2). However, this difference was not observed over time between groups (interaction $P = .5844$). After adjustment for graft type, age, BMI, sex, smoking status, and depression, the multimodal nonopioid group demonstrated lower mean pain levels, measured via the VAS scale, than did the opioid group (mean difference, 1.71; 95% CI, 1.49 to 1.93; $P < .001$). However, no significant differences were seen between the 2 groups' mean pain levels over time (interaction $P = .5708$) (Figure 3). Regarding the PROMIS PI-SF, 2-sample t tests demonstrated that there was no significant difference in patients' preoperative scores (opioid group, 58.6 ± 7.9; multimodal nonopioid group, 57.5 ± 7.4; $P = .385$) and postoperative scores (opioid group, 66.3 ± 8.2; multimodal nonopioid group, 61.4 ± 8.8; $P = .147$). Furthermore, after adjustment for age, sex, BMI, smoking status, and depression, the mixed-models repeated-measures analysis demonstrated no significant difference in PROMIS PI-SF scores between the 2 study groups (mean difference, 3.27; 95% CI, –0.86 to 7.39; $P = .1184$) and no significant difference over time (interaction $P = .3154$) (Figure 4). Patients using opioid analgesia reported the highest rates of consumption on

TABLE 2
Characteristics of Patients Using Opioid and Multimodal Nonopioid Analgesia Postoperatively[a]

	Included Patients (n = 62)	Opioid Group (n = 28)	Multimodal Nonopioid Group (n = 34)	*P* Value
Age, y	27.3 ± 12.7	27.4 ± 12.4	27.2 ± 13.1	.676
Sex				.856
Male	34 (55)	15 (54)	19 (56)	
Female	28 (45)	13 (46)	15 (44)	
Race				.389
White	25 (42)	12 (46)	13 (38)	
African American	7 (12)	4 (15)	15 (44)	
Hispanic	1 (2)	0 (0)	1 (3)	
Asian	3 (5)	2 (8)	1 (3)	
Other	14 (23)	8 (31)	16 (47)	
Body mass index	27.5 ± 4.6	27.3 ± 5.2	27.7 ± 4.2	.497
Smoker				.116
Yes	7 (11)	1 (4)	6 (18)	
No	55 (89)	27 (96)	28 (82)	
Depression				.366
Yes	5 (8)	1 (4)	4 (12)	
No	57 (92)	27 (96)	30 (88)	
Graft type				.394
Bone–patellar tendon–bone	39 (63)	16 (57)	23 (68)	
Hamstring	23 (37)	12 (43)	11 (32)	
Meniscal repair				.756
Yes	13 (21)	5 (18)	8 (24)	
No	49 (79)	23 (82)	26 (76)	
Meniscectomy				.678
Yes	35 (56)	15 (54)	20 (59)	
No	27 (44)	13 (46)	14 (41)	
Nerve block				.320
Adductor	58 (94)	25 (89)	33 (97)	
Femoral	4 (6)	3 (11)	1 (3)	

[a]Values are expressed as mean ± SD or n (%).

postoperative day (POD) 1 (2 pills [range, 1.5-3 pills]; 13.1 ± 8.0 MME) and POD 2 (2.5 pills [range, 1.75-4 pills]; 15.2 ± 11.3 MME) and the lowest rates of consumption on POD 9 (1 pill [range, 0-1 pills]; 4.3 ± 4.7 MME) and POD 10 (1 pill [range, 0-2 pills]; 6.7 ± 7.5 MME) (Figure 5).

Female patients had higher preoperative PROMIS PI-SF scores compared with males (60.9 ± 4.7 vs 56.1 ± 8.5, respectively; $P = .03$), but no significant differences in VAS pain scores or opioid consumption after surgery were seen between male and female patients (interaction $P = .9995$). Additionally, no significant differences were noted over time in pain scores or total narcotic consumption based on graft type or concomitant meniscal procedures (interaction $P = .9978$ and $P = .9945$, respectively). Pearson correlation analysis demonstrated African American patients to have a low correlation with VAS pain on POD 1 through 10 ($r = 0.30$ to 0.50; $P < .05$), whereas there was no correlation in White patients ($r = -0.10$ to 0.28; $P > .05$).

Adverse Events

We found no differences between groups regarding the number of days that patients reported gastrointestinal symptoms, drowsiness, or dizziness ($P > .05$) (Table 3). As well, we noted no significant difference in the number of days reported without side effects (opioid group, 3.6 ± 4.0 days; multimodal nonopioid group, 4.9 ± 3.5 days; $P = .218$). The most common side effects for both the opioid and multimodal nonopioid pain protocol groups were drowsiness and constipation. No intraoperative or postoperative complications were encountered during this study (ie, deep vein thrombosis or surgical site infections). All patients (100%) in the multimodal nonopioid protocol group stated they were satisfied with their pain management. No complications were reported for the multimodal nonopioid protocol group, and no patients required emergency opioid analgesia.

DISCUSSION

This single-center RCT compared pain control after ACLR using multimodal nonopioid and opioid pain regimens. The study found that a multimodal nonopioid postoperative analgesic protocol provided at least equivalent pain control and satisfaction compared with a traditional opioid regimen. Given the opioid epidemic, these results suggest that a multimodal nonopioid pain protocol may be a suitable alternative to opioid analgesia for pain management after ACLR.

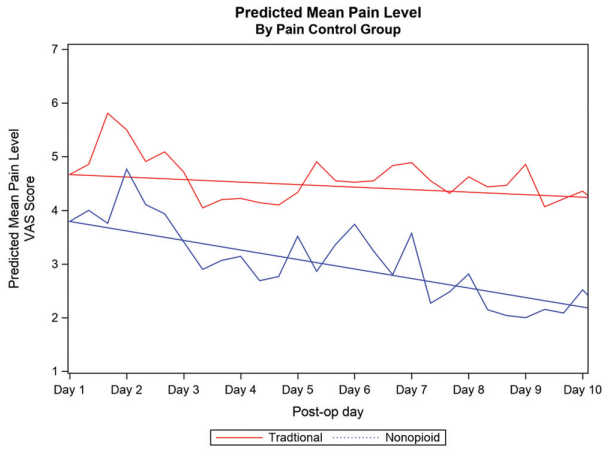

Figure 2. Mean daily pain data unadjusted, comparing daily pain levels between the 2 groups. No significant difference in pain levels was found between the 2 groups over time (interaction $P = .5844$). VAS, visual analog scale. Postop day indicates days after surgery.

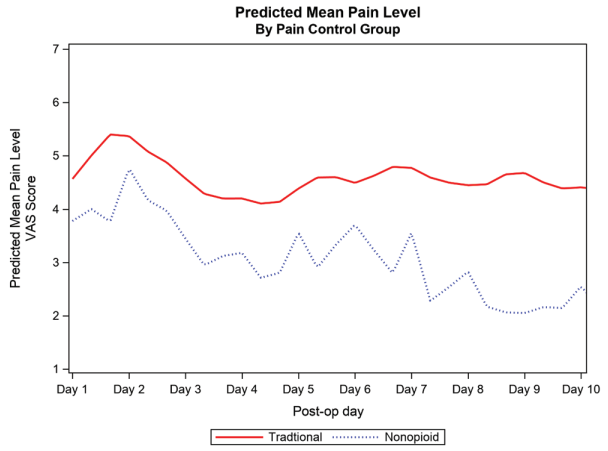

Figure 3. Mean daily pain data controlling for age, graft, body mass index, sex, smoking, and depression, comparing daily pain levels between the 2 groups. No significant difference in pain levels was found between the 2 groups over time (interaction $P = .5708$). VAS, visual analog scale. Postop day indicates days after surgery.

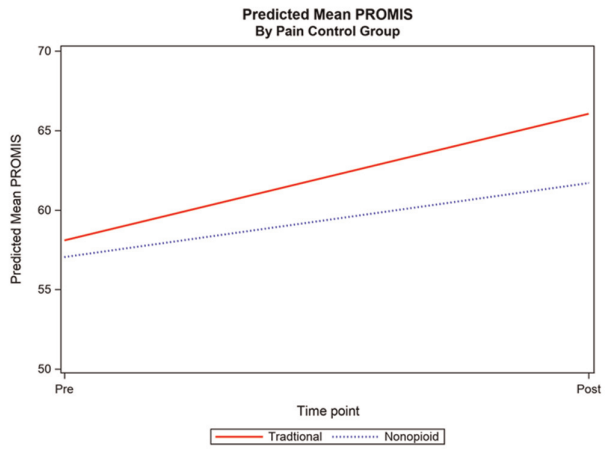

Figure 4. Patient-Reported Outcomes Measurement and Information System Pain Interference Short Form (PROMIS PI-SF) scores controlling for age, sex, body mass index, smoking, and depression. No significant difference in PROMIS PI-SF scores was found between the 2 groups over time (preoperative [pre] to postoperative [post]; interaction $P = .3154$).

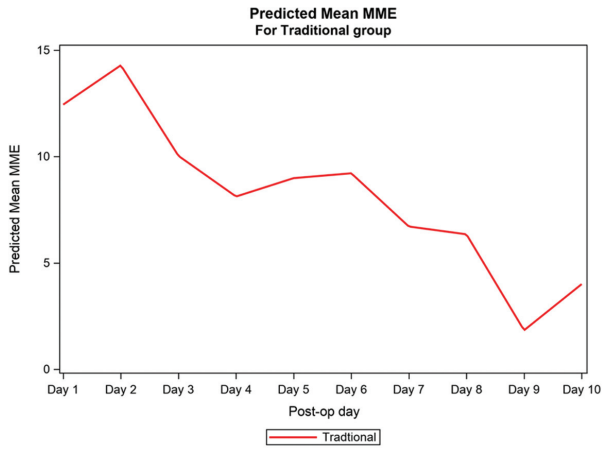

Figure 5. Predicted mean morphine milligram equivalents (MME) for opioid users, controlling for age, sex, body mass index, smoking, and depression. MME decreased as time from surgery increased. Postop day indicates days after surgery.

Positive results were previously demonstrated in studies that evaluated multimodal protocols in the context of ACLR. In an RCT investigating the use of gabapentin as a preoperative adjunct to ACLR, Menigaux et al[18] found that cumulative morphine consumption in the first 48 hours was reduced by half among patients administered gabapentin. In a double-blinded RCT, Barber and Gladu[2] investigated the analgesic effectiveness of ketorolac compared with hydrocodone and acetaminophen for pain relief after ACLR and found that ketorolac significantly improved pain relief in the acute postoperative period. Last, in a case series of 141 patients (49 ACLRs) using a multimodal nonopioid pain protocol identical to that used in the current study, Moutzouros et al[19] found that 45% of all patients did not require any breakthrough opioids for pain control, and the mean VAS pain score at 1 week postoperatively was 3.6 ± 2.0. The findings of the present study demonstrated that similar pain control and patient satisfaction can be achieved after ACLR without the use of narcotic medication.

One of the major challenges of postoperative analgesia entails optimizing therapeutic effects while minimizing

TABLE 3
Side Effects in Opioid and Multimodal Nonopioid Pain Protocol Groups[a]

Variable	Response	Opioid Group (n = 28)	Multimodal Nonopioid Group (n = 34)	*P* Value	Duration, d, Opioid Group (n = 28)	Duration, d, Multimodal Nonopioid Group (n = 34)	*P* Value
Constipation	Yes	13 (65)	12 (55)	.491	2.5 ± 3.5	1.1 ± 2.2	.152
	No	7 (35)	10 (45)				
Nausea	Yes	10 (56)	9 (43)	.429	0.8 ± 1.0	0.6 ± 1.1	.285
	No	8 (44)	12 (57)				
Diarrhea	Yes	2 (15)	2 (11)	≥.999	0.1 ± 0.3	0.1 ± 0.3	.819
	No	11 (85)	17 (89)				
Upset stomach	Yes	8 (50)	9 (43)	.666	0.5 ± 0.9	0.8 ± 2.0	.726
	No	8 (50)	12 (57)				
Drowsy	Yes	12 (67)	18 (72)	.707	2.4 ± 3.3	2.8 ± 3.5	.563
	No	6 (33)	7 (28)				
Loopy	Yes	4 (29)	12 (55)	.126	0.6 ± 2.0	1.1 ± 2.0	.090
	No	10 (71)	10 (45)				

[a]Values are expressed as n (%) or mean ± SD.

adverse effects. A survey study of 618 patients found that drowsiness was the most commonly reported opioid-related side effect (78% of patients), but patients were significantly more concerned by gastrointestinal side effects.[10] In a case series reporting on the side effects of the current multimodal nonopioid protocol, Moutzouros and colleagues[19] found that 53.6% of patients did not report any side effects at the first postoperative appointment. However, 23.5% of patients reported drowsiness and 15.7% of patients reported dizziness. In the present study, no differences in daily reported side effects were found between the multimodal nonopioid and opioid groups, suggesting similar side effect profiles. Narcotic medication is a known cause of drowsiness after surgery. It is possible that the use of diazepam, and to a lesser extent gabapentin, was responsible for drowsiness in the multimodal nonopioid group. Substitution with other muscle-relaxing agents such as methocarbamol or cyclobenzaprine may reduce these effects. Overall, the findings of this study demonstrated that the nonopioid multimodal protocol can effectively control pain without causing significant side effects compared with traditional opioid pain management.

With respect to patient characteristics, a meta-analysis by Kim et al[14] found that African American patients had higher pain sensitivity compared with non-Hispanic White patients, specifically showing lower pain tolerance (standard mean difference [SMD], –0.64; 95% CI, −0.80 to −0.48) and higher ratings for pain intensity and unpleasantness (SMD, 0.37; 95% CI, 0.19 to 0.54). In a systematic review, Rahim-Williams and colleagues[23] also found that African American patients had lower pain tolerance and higher ratings of suprathreshold stimuli compared with non-Hispanic White patients. In the present study, African American patients exhibited a significant but low correlation with VAS pain scores at each postoperative time point. The literature has suggested that ethnic differences may not be fully attributable to socioeconomic and cultural differences but may be due to genetics, nociceptive reflexes, and other neurobiological processes.[3,4,11,16,26] It is possible that the present study was not powered to adequately evaluate the influence of psychosocial factors on pain perception; however, the present findings suggest an association between race and pain in the context of ACLR that merits further investigation.

Limitations

Patients were aware of the medicines they were taking, and knowledge of the treatment may have led to cognitive bias; however, data were recorded by a blinded observer with no knowledge of patient randomization in order to eliminate associated statistical bias. Patients were not blinded in this study because of the importance of education and monitoring for adverse events, which was crucial to patient safety with a new pain protocol consisting of several medications taken in combination. For these reasons, it was not feasible to use a double-blinded strategy. Furthermore, measuring patient compliance in the study was relatively difficult to implement without adding to patient burden. Similarly, patients were not asked whether they had supplemented their assigned pain regimen with other home medications or therapies. Patients had preoperative counseling stressing the importance of compliance, but it is unknown whether patients used other multimodal agents or self-obtained opioids. It is important to mention that 19 patients screened for eligibility in the study declined to participate. This was a considerable number, but the reasons for opting out of the study were not systematically collected in order to avoid increasing an already taxing battery of patient questionnaires and tasks. It is possible that these patients declined to participate in order to ensure they received optimal pain control, including opioids if necessary, which could affect the generalizability of this investigation. The study was not powered to detect differences in side effect incidence, function, mental status, postoperative complications, change in opioid consumption (MME) over time, or long-term pain and disability past 10

days postoperatively. Additionally, the 10-day follow-up limited the ability to detect longer term differences in pain control and side effects between groups. A subgroup analysis based on psychosocial variables that may influence pain and opioid intake was not performed, and a larger cohort would be needed for such an analysis. All patients received a peripheral nerve block, and this procedure has inherent risks and side effects that were not specifically evaluated. Last, due to ethical considerations regarding postoperative pain control, the total magnitude of pain improvement could not be measured; however, patients given the standard-of-care opioid postoperative analgesia served as a comparative cohort from which conclusions can be made. Although a variety of opioid regimens are available, patients in this trial were given the most common opioid regimen at our institute (hydrocodone-acetaminophen) on an as-needed basis. This introduced some variability in comparison of dosing strategies (as-needed in the opioid protocol vs scheduled in the multimodal nonopioid protocol) but provided a comparison to the most commonly prescribed opioid medication in the United States.[21]

CONCLUSION

This study found that a multimodal nonopioid pain protocol provided at least equivalent pain control compared with traditional opioid analgesics in patients undergoing ALCR. Minimal side effects, which did not differ between groups, were noted, and all patients reported satisfaction with their pain management.

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