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A Multimodal Pain Management Protocol Including Preoperative Cryoneurolysis for Total Knee Arthroplasty to Reduce Pain, Opioid Consumption, and Length of Stay

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ABSTRACT

Background: A retrospective analysis was conducted to determine if cryoneurolysis of superficial genicular nerves combined with standard care decreased postoperative opioids and pain after total knee arthroplasty (TKA).

Methods: Data from patients who underwent TKA at a single center were analyzed. Patients who received standardized cryoneurolysis before TKA were compared with a historical control group including patients who underwent TKA without cryoneurolysis. Both groups received a similar perioperative multimodal pain management protocol. The primary outcome was opioid intake at various time points from hospital stay to 6 weeks after discharge. Additional outcomes included pain, length of stay, and range of motion.

Results: The analysis included 267 patients (cryoneurolysis group: n = 169; control group: n = 98). During the hospital stay, the cryoneurolysis group had 51% lower daily morphine milligram equivalents (MMEs) (47 vs 97 MMEs; ratio estimate, 0.49 [95% confidence interval (CI), 0.43-0.56]; $P < .0001$) and 22% lower mean pain score (ratio estimate, 0.78 [95% CI, 0.70-0.88]; $P < .0001$) vs the control group. The cryoneurolysis group received significantly fewer cumulative MMEs, including discharge prescriptions, than the control group at week 2 (855 vs 1312 MMEs; ratio estimate, 0.65 [95% CI, 0.59-0.73]; $P < .0001$) and week 6 (894 vs 1406 MMEs; ratio estimate, 0.64 [95% CI, 0.57-0.71]; $P < .0001$). The cryoneurolysis group had significant 44% reduction in overall length of stay ($P < .0001$) and greater flexion degree at discharge ($P < .0001$).

Conclusions: Addition of preoperative cryoneurolysis to a multimodal pain management protocol reduced opioids and in-hospital pain and optimized outcomes during the 6-week recovery period after TKA.

Introduction

Management of pain is an important part of patient care after primary total knee arthroplasty (TKA). Although opioid analgesics have long been the mainstay of postoperative pain therapy, these agents cause significant adverse effects, including respiratory complications, falls, nausea, vomiting, constipation, urinary retention, and cognitive impairment [1], which significantly increase hospital costs and length of stay (LOS) [2]. Increasingly, physicians and patients have been concerned about the long-term implications of taking opioids to treat pain after TKA. Although patients who take opioids before TKA reduce their use of opioids after surgery [3], a substantial proportion of patients (range, 10%-82%) undergoing primary TKA remain or become long-term opioid users after surgery (ie, opioid prescriptions filled ≥90 days after surgery) [4-10], and 15% of patients undergoing TKA develop opioid dependence [11]. Prolonged postoperative use of opioids after TKA is associated with significantly increased rates of infection, stiffness, ipsilateral knee arthroscopy or TKA, and revision arthroplasty [4,8,9].

A recent review suggested that several studies of patients undergoing a variety of procedures have demonstrated that the presence and intensity of acute postoperative pain are significant predictive risk factors for the development of chronic pain and that postoperative pain adversely affects physical functioning, recovery,

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and quality of life [12]. Given that there is a need to better control postoperative pain while reducing use of opioids, hospitals and surgeons have implemented multimodal pain protocols with positive effects including decreases in respiratory and gastrointestinal complications and opioid prescriptions [13]. Novel modalities that can reduce opioid requirements have the potential to enhance postoperative recovery and improve patient outcomes after total joint replacement [14].

Clinical trial and retrospective data have indicated that a multimodal pain management protocol that included preoperative cryoneurolysis of the superficial genicular nerves reduced opioid consumption without increasing pain for up to 12 weeks after TKA compared with a standard multimodal pain management protocol [15,16]. In clinical trials, cryoneurolysis has been shown to be associated with mostly mild adverse events, suggesting it is a safe option for pain control [15,17]. The purpose of this retrospective study was to evaluate the effect of a change to a multimodal pain management protocol to include preoperative cryoneurolysis on postoperative opioid use and pain after TKA at a single center. On the basis of results from prior studies, we hypothesized that, compared with a control group receiving a standard multimodal pain protocol without preoperative cryoneurolysis, the use of preoperative cryoneurolysis would result in significant reductions in opioid use (in-hospital consumption and postdischarge prescriptions) as well as improvements in hospital LOS, patient-reported pain scores, and postoperative range of motion.

Material and methods

Study design

This was a retrospective chart review of patients who underwent inpatient primary TKA by a single surgeon at a private orthopedic practice. The control group consisted of consecutive patients treated from January 2017 to December 2017 who received a standard multimodal pain protocol that did not include preoperative cryoneurolysis. In 2018, the practice added preoperatively administered cryoneurolysis to their multimodal pain regimen for TKAs. However, because this transitory period included protocol optimization (eg, selection of needle administration tip for cryoneurolysis, optimization and training on the ultrasound-guided technique for identifying the femoral cutaneous nerves, modifications to the timing of lidocaine administration at the cryoneurolysis site) and not all patients received the same multimodal pain management regimen, this period was not considered reliable for comparisons of cryoneurolysis vs prior standard of care. As a result, the cryoneurolysis group in this study included patients treated from February 2019 to June 2020, when the practice began administering optimized preoperative cryoneurolysis to all patients undergoing TKA as part of its standard multimodal perioperative pain protocol. Five patients during the 2019-2020 window did not receive cryoneurolysis because their insurance would not cover the procedure and the patients declined out-of-pocket payment.

The standard multimodal pain pathway used in this study included preoperative components (oral meloxicam 7.5 mg, oral extended-release oxycodone 10 mg, oral acetaminophen 1000 mg, scopolamine patch 1.5 mg, oral gabapentin 600 mg, and oral aprepitant 40 mg if the patient was scheduled to leave on the same day as the surgery), perioperative components (single-shot adductor canal block with ropivacaine and spinal anesthesia with bupivacaine 0.75% with dextrose or general anesthesia in patients with extensive arthritis or spine fusion, and a periarticular mixture consisting of morphine 5 mg, toradol 15 mg, sodium chloride 0.9% 40 mL, ropivacaine 0.5% 80 mg, and epinephrine 0.3 mg), and in-hospital postoperative components, including those prescribed upon discharge (oral acetaminophen 500 mg every 6 hours, oral meloxicam 7.5 mg twice daily, oral tramadol 50 mg every 6 hours as needed for pain, oral oxycodone 5 mg every 3 hours as needed for breakthrough pain, and oral morphine 15 mg twice daily as needed for pain for patients aged $\leq$65 years). This study received institutional review board approval.

Cryoneurolysis was administered using the iovera° device (Pacira CryoTech, Inc., Fremont, CA) via a SmartTip that consisted of a single 20-gauge, 90-mm closed-end needle. The iovera° device uses the well-established principle that localized exposure to controlled, moderately low temperature conditions can alter nerve function [18]. Cryogen (nitrous oxide) flows from the disposable cartridge through the handpiece to the SmartTip, and a highly localized cold zone is formed via the Joule-Thomson effect when the nitrous oxide enters the needles [15,18,19]. Nothing is injected, and the nitrous oxide gas is vented safely out of the handpiece.

Cryoneurolysis was administered to conscious patients after local anesthesia. The specific treatment targets were the infrapatellar branches of the saphenous nerve near the knee and branches of the femoral cutaneous nerves in the mid-to-distal anterior thigh, which were identified with the use of ultrasonography. After the nerves were mapped, an 89-mm (3.5-inch), 20-gauge spinal needle was advanced to the nerve under ultrasound, and ~1 mL of 1% lidocaine was injected around the nerve at the site intended for cryoneurolysis. The 90-mm SmartTip probe was then inserted under ultrasound guidance to contact the superior aspect of the target nerve, and cryoneurolysis was administered. The cycle ran for approximately 1 minute and 45 seconds, during which time patient feedback was recorded.

Outcome measures

The primary outcome of this study was opioid intake at various time points from hospital stay to 6 weeks after discharge. Measurements of opioid intake included mean total and daily morphine milligram equivalents (MMEs) during the hospital stay, mean total opioids in MMEs prescribed at discharge and at the week-2 and week-6 follow-up visits, cumulative opioid prescriptions in MMEs at week 2 and week 6 (including opioids prescribed at earlier time points such as at discharge), and the proportion of patients with $\geq$1 opioid prescription at discharge and the week-2 and week-6 follow-up visits. Patients lacking opioid intake information during the study period were excluded. Additional outcomes included pain scores assessed using an 11-point numerical rating scale (where 0 = no pain and 10 = worst pain possible) measured during the hospital stay, LOS, and range-of-motion scores at and after discharge. Mean pain scores during hospitalization and maximum pain scores reported at any time point during hospitalization were compared between groups.

Statistical analysis

The mean and frequency were calculated for each outcome, and an appropriate statistical test (Student's *t*-test or chi-square test) was used to evaluate differences between the cryoneurolysis and control groups. In addition, a generalized linear model was performed with gamma distribution and log link function for continuous outcomes and binomial distribution and logit link function for binary outcomes. The model was adjusted for age, sex, American Society of Anesthesiologists (ASA) physical status classification, body mass index (BMI), and prior opioid exposure (defined as having an opioid listed on their home medication documentation). A 2-sided P value < .05 was considered statistically significant. All analyses were performed using SAS, version 9.4 (SAS Institute Inc., Cary, NC).

Table 1
Baseline patient demographics and characteristics.

	Cryoneurolysis group (n = 169)	Control group (n = 98)	*P*
Age, mean (SD), y	66 (9)	68 (9)	.1696
Female, n (%)	100 (59)	65 (66)	.2461
ASA physical status classification, n (%)			.1444
I	10 (6)	12 (12)	
II	120 (71)	61 (62)	
III	39 (23)	25 (26)	
BMI,[a] mean (SD), kg/m^2	29 (4)	31 (5)	.0015
No prior exposure to opioids, n (%)	162 (96)	79 (81)	<.0001

SD, standard deviation.
[a] BMI data were missing for 1 patient in the control group.

Results

Baseline demographics and characteristics

A total of 267 patients were included in the analysis (169 patients in the cryoneurolysis group and 98 patients in the control group). Patients in the cryoneurolysis group received cryoneurolysis a median of 9 days (interquartile range, 8-11 days) before the TKA procedure. The groups had a mean age range of 66-68 years and were likely to be female (range, 59%-66%; Table 1). The ASA physical status classifications of the 2 groups were similar. Compared with the control group, the mean BMI was significantly lower in the cryoneurolysis group, although the difference was small (29 vs 31 kg/m^2). In addition, a significantly greater proportion of patients in the cryoneurolysis vs control group had no prior exposure to opioids (96% vs 81%).

Opioid consumption

All patients in both groups received an opioid prescription at discharge, with patients in the cryoneurolysis group receiving significantly fewer MMEs at discharge than the control group (Table 2). The cryoneurolysis group received significantly fewer cumulative MMEs (including opioids prescribed at earlier time points such as at discharge) vs the control group at week 2 (adjusted mean MMEs: 855 vs 1312; ratio estimate, 0.65 [95% CI, 0.59-0.73]; $P < .0001$) and at week 6 (adjusted mean MMEs: 894 vs 1406; ratio estimate, 0.64 [95% CI, 0.57-0.71]; $P < .0001$), reflecting 35% and 36% reductions in opioid intake, respectively. At week 2 after discharge, a significantly greater proportion of patients in the cryoneurolysis group received ≥1 opioid prescription than the control group (51% vs 26%). However, there was no significant difference between groups in the proportion of patients who received ≥1 opioid prescription at week 6.

During the hospital stay, the cryoneurolysis group also had 68% less consumption of total opioids in MMEs than the control group ($P < .0001$); this was not solely driven by a longer LOS, as indicated by the cryoneurolysis group also having 51% less daily MME intake than the control group ($P < .0001$).

Pain assessment, LOS, and range of motion

The cryoneurolysis group had a significant 22% reduction in adjusted mean pain scores during their hospital stay compared with the control group and was 62% less likely to have a mean pain score ≥4 (Table 3). Compared with the control group, the cryoneurolysis group had a significantly reduced overall LOS ($P < .0001$). In the cryoneurolysis group, 17% of patients had an overall LOS ≥2 days, compared with 99% of patients in the control group ($P < .0001$).

At discharge, patients in the cryoneurolysis group exhibited greater range of motion than patients in the control group, as indicated by significantly greater adjusted mean flexion degree, a higher proportion of patients achieving flexion ≥90°, significantly lower adjusted mean extension degree, and a higher proportion of patients with extension ≤5° (Table 4). Flexion degree and extension degree were similar between the 2 groups at week 2 and at week 6 after discharge, apart from significantly improved adjusted mean extension scores and a higher proportion of patients achieving extension ≤2.5° in the cryoneurolysis group at week 6.

Safety

In the present study, no infections occurred in the cryoneurolysis group. Side effects experienced by all patients included numbness in the area of treated nerves, which was considered desirable given the upcoming surgical incision and dissection. Dysesthesia, described by patients as a tingling electrical sensation, occurred in all patients, consistent with the mechanism of action of cryoneurolysis; that is, a reversible injury to targeted nerves [20]. In

Table 2
Opioid use after TKA.[a]

	Cryoneurolysis group (n = 169)	Control group (n = 98)	Ratio estimate (95% CI)	*P*
In hospital				
Total MMEs, adjusted mean (95% CI)	104 (89-122)	324 (279-376)	0.32 (0.28-0.37)	<.0001
Daily MMEs, adjusted mean (95% CI)	47 (41-54)	97 (85-111)	0.49 (0.43-0.56)	<.0001
At discharge				
≥1 prescription, n (%)	169 (100)	98 (100)	NA[b]	–
Total MMEs, adjusted mean (95% CI)	660 (593-736)	1154 (1044-1277)	0.57 (0.52-0.63)	<.0001
At week-2 follow-up visit				
≥1 prescription, n (%)	86 (51)	26 (26)	3.51 (1.90-6.51)	<.0001
Total MMEs, adjusted mean (95% CI)	203 (114-361)	115 (64-208)	1.76 (1.00-3.11)	.0509
Cumulative MMEs at week 2,[c] adjusted mean (95% CI)	855 (765-957)	1312 (1182-1457)	0.65 (0.59-0.73)	<.0001
At week-6 follow-up visit				
≥1 prescription, n (%)	20 (12)	20 (20)	0.61 (0.29-1.28)	.1936
Total MMEs, adjusted mean (95% CI)	34 (19-62)	87 (48-159)	0.39 (0.22-0.69)	.0012
Cumulative MMEs at week 6,[c] adjusted mean (95% CI)	894 (795-1004)	1406 (1260-1570)	0.64 (0.57-0.71)	<.0001

NA, not applicable.
[a] Model adjusted for age, sex, ASA physical status classification, BMI, and prior opioid exposure.
[b] Ratio estimate could not be calculated because all patients in both groups received ≥1 prescription at discharge.
[c] Including opioids prescribed at earlier time points such as at discharge.

Table 3
Pain scores during the hospital stay and LOS.[a]

	Cryoneurolysis group (n = 169)	Control group (n = 98)	Ratio estimate (95% CI)	*P*
Pain score, adjusted mean (95% CI)	3.06 (2.71-3.46)	3.92 (3.49-4.40)	0.78 (0.70-0.88)	<.0001
Maximum pain score, adjusted mean (95% CI)	6.68 (6.18-7.23)	8.21 (7.63-8.85)	0.81 (0.75-0.88)	<.0001
Mean pain score ≥4, n (%)	25 (15)	36 (37)	0.38 (0.20-0.72)	.0031
Overall LOS, adjusted mean (95% CI), d	1.42 (1.16-1.74)	2.52 (2.12-2.99)	0.56 (0.47-0.68)	<.0001
LOS ≥2 d, n (%)	29 (17)	97 (99)	0.001 (0.0001-0.08)	<.0001

[a] Pain scores measured on a 0-10 numerical rating scale. Model adjusted for age, sex, ASA physical status class, BMI, and prior opioid exposure.

most cases, dysesthesia was considered tolerable without disruption of activities of daily living or sleep. A more severe form of these dysesthesia symptoms can occur after cryoneurolysis, in the authors' experience, typically 2-14 days afterward, and are attributable to a partially treated or frozen nerve [20]. This severe form of dysesthesia was described as burning in the area of the nerve that interferes with activities of daily living and sleep. Severe dysesthesia occurred in 2 participants in the cryoneurolysis group (1.2%).

Discussion

In this retrospective study, changing a multimodal pain protocol for TKA to include preoperative cryoneurolysis was associated with decreases in opioid consumption during hospitalization and cumulative opioid prescriptions up to 6 weeks after discharge (including prescriptions at discharge), as well as a statistically significant reduction in acute pain during hospitalization. Compared with the control group, the cryoneurolysis group reported lower adjusted mean and maximum pain scores during hospitalization, was 62% less likely to have a mean pain score ≥4 during hospitalization, had a 1.1-day shorter LOS, consumed fewer opioids during hospitalization, and received significantly fewer opioids via prescriptions at discharge and significantly fewer cumulative opioid prescriptions at week 2 and week 6. Together, these findings indicate that the analgesic benefits of cryoneurolysis contributed to superior pain control both during the acute or inpatient and short-term postoperative periods.

From the in-hospital data showing significantly lower pain scores and in-hospital opioid consumption in the cryoneurolysis group relative to controls, we conclude patients who received cryoneurolysis had less pain and therefore had reduced opioid requirements at discharge. This is also consistent with results showing that these patients received significantly fewer total MMEs and a smaller prescribed dose of opioids at discharge than controls. Although significantly more patients in the cryoneurolysis group required refills at the week-2 follow-up visit, the cumulative total MMEs for postsurgical analgesia were significantly lower in the cryoneurolysis group than those in the control group through both week 2 and week 6 after discharge. The increased refill rate could be explained by the cryoneurolysis group receiving a reduced opioid prescription volume at discharge vs the control group (mean total MMEs at discharge, 660 vs 1154). We believe that the pronounced tapering of opioid prescriptions at 6 weeks in the cryoneurolysis group is important, given that data from a retrospective observational study have suggested that prolonged postoperative use of opioids is associated with a greater risk of developing opioid misuse [21].

Controlling pain after TKA while reducing opioid consumption is important. Patients undergoing TKA who experience moderate-to-severe acute postoperative pain are more likely to develop long-term opioid use after surgery [22]. The potential of cryoneurolysis to reduce acute pain while allowing for less opioid use may prevent the development of chronic pain and long-term opioid use or dependence in these patients. The shorter LOS and lower cumulative opioid prescription volume observed with a standard

Table 4
ROM after TKA.[a]

	Cryoneurolysis group	Control group	Ratio estimate (95% CI)	*P*
At discharge				
Number of patients with ROM data, n	168	95	–	–
Flexion degree, adjusted mean (95% CI)	104 (102-106)	91.5 (90-93)	1.14 (1.11-1.16)	<.0001
Flexion ≥90°, n (%)	165 (98)	78 (80)	11.72 (3.56-38.55)	<.0001
Extension degree, adjusted mean (95% CI)	3.83 (3.37-4.35)	4.57 (4.04-5.18)	0.84 (0.74-0.94)	.0037
Extension ≤5°, n (%)	164 (97)	77 (79)	10.83 (3.68-31.92)	<.0001
At week 2				
Number of patients with ROM data, n	158	91	–	–
Flexion degree, adjusted mean (95% CI)	107 (103-110)	103 (100-107)	1.03 (1.00-1.07)	.0501
Flexion ≥90°, n (%)	149 (88)	84 (87)	0.95 (0.42-2.16)	.9117
Extension degree, adjusted mean (95% CI)	4.44 (3.68-5.36)	4.61 (3.92-5.44)	0.96 (0.80-1.16)	.6855
Extension ≤5°, n (%)	164 (97)	91 (94)	1.73 (0.44-6.86)	.4332
At week 6				
Number of patients with ROM data, n	160	94	–	–
Flexion degree, adjusted mean (95% CI)	124 (121-126)	123 (121-126)	1.00 (0.98-1.02)	.6787
Flexion ≥90°, n (%)	161 (95)	93 (96)	1.28 (0.34-4.88)	.7144
Flexion ≥115°, n (%)	145 (86)	87 (90)	0.61 (0.26-1.47)	.2712
Extension degree, adjusted mean (95% CI)	2.11 (1.61-2.77)	4.14 (3.21-5.34)	0.51 (0.38-0.68)	<.0001
Extension ≤5°, n (%)	160 (100)	87 (93)	NA[b]	–
Extension ≤2.5°, n (%)	141 (88)	67 (71)	2.61 (1.27-5.40)	.0094

NA, not applicable; ROM, range of motion.
[a] Model adjusted for age, sex, ASA physical status class, BMI, and prior opioid exposure.
[b] Ratio estimate could not be calculated because all patients in the cryoneurolysis group had an extension degree ≤5°.

multimodal pain protocol with vs without cryoneurolysis suggest cryoneurolysis could provide benefits by reducing inpatient health-care costs associated with TKA; a large administrative claims data analysis showed that filling an outpatient opioid prescription during the year following inpatient or outpatient surgery was associated with increased health-care costs and utilization [23].

We note that actual opioid consumption may have differed from presumed opioid consumption derived from prescription data. However, patients in the cryoneurolysis group received significantly fewer total MMEs at discharge, and differences in cumulative MMEs were maintained at weeks 2 and 6. Moreover, there was a significant 61% reduction in total MMEs at week 6.

With regard to safety, cryoneurolysis was generally associated with numbness and dysesthesia. Mild dysesthesia is expected after cryoneurolysis and, along with other potential side effects, is typically self-limiting [17]. In the present study, dysesthesia did not interfere with activities of daily living or sleep, except in 2 participants who experienced severe dysesthesia. Although resolution of dysesthesia was not documented and is beyond the scope of this study, in the authors' experience, altered sensations may last for up to 4-6 months. Dysesthesia resolves when nerve regeneration is complete, resulting in a full return of sensory function and a resolution of numbness. The timing of complete nerve regeneration is dependent on the ability of a nerve to regenerate from the site of insult (ie, frozen zone) to its terminal receptors, and that rate has been suggested in the literature to be approximately 1 mm/day [24]. Retreatment of the offending nerve 1-2 cm proximal to the original treatment site, focusing on a complete envelopment of the nerve within the ice ball, can be used for more immediate resolution of these severe symptoms. Although generally considered safe [15,17], education on dysesthesia and other potential side effects of cryoneurolysis is important to set realistic patient expectations of their surgical experiences.

There were a few limitations to this study. First, this study was retrospective and therefore patients were not randomized between treatments. These factors preclude the ability to determine causality, given that it was possible that variables other than the addition of cryoneurolysis to a multimodal pain protocol may have contributed to the observed reductions in pain and opioid consumption. When the practice in this study began to use cryoneurolysis in 2018, there was limited information on its use in TKA, which necessitated ongoing protocol refinement and optimization, including optimization of the ultrasound-guided technique for identifying the femoral cutaneous nerves and changes in the type of needle tip used to administer cryoneurolysis. Because of this changing of the cryoneurolysis protocol over time, TKA procedures conducted in 2018 were excluded from the current analysis to enable more reliable comparisons between patients treated with vs without a standardized cryoneurolysis procedure. This approach resulted in a time gap between the cryoneurolysis group (2019-2020) and the comparator control group (2017). However, no relevant changes were made to the multimodal protocol over this time period. Of note, the adjusted mean total opioid prescription at discharge was significantly lower in the more contemporary cryoneurolysis group (2019-2020) than that in the control group (2017); as such, changes in opioid-prescribing patterns over time (eg, greater awareness of risks of opioids, greater understanding that lower doses of opioids can provide effective analgesia) could have impacted the opioid prescription outcomes. However, it is the opinion of the authors that this was unlikely because the practice did not formally alter their opioid-prescribing policy over this time period, and the lower pain scores and opioid consumption observed during the hospital stay in the cryoneurolysis vs the control group were consistent with reduced opioid requirements at discharge in the cryoneurolysis group compared with the control group. Ultimately, even if opioid reductions between the cryoneurolysis and control groups were influenced by greater awareness of the need to reduce opioid prescriptions, the short-term pain outcomes and long-term functional outcomes with cryoneurolysis were optimized, which supports the effectiveness of cryoneurolysis in managing pain and optimizing recovery. Second, it is possible that a trend toward reduced LOS after TKA may partially explain the significant reduction in LOS for the patients who received cryoneurolysis compared with the control group, given that the patients who received cryoneurolysis were treated >1 year later. Third, limited preoperative data were available for the study sample, and preoperative opioid use, which is a strong predictor of the amount and duration of postoperative opioid use after TKA [25], may not have been fully captured; this may have affected the ability to reliably assess for between-group differences in this potentially confounding variable. Of note, a greater proportion of patients in the cryoneurolysis group in 2019-2020 (96%) had no prior opioid exposure compared with the control group from 2017 (81%). It is the opinion of the authors that this trend could be in part related to a decreased likelihood of primary care providers to prescribe opioids for osteoarthritis pain control over time because of increased awareness of the opioid epidemic. Because it is not possible to determine if preoperative exposure may have played a role in the significant difference between groups in opioid prescriptions at the 2-week follow-up, further study is needed to determine the influence of preoperative opioid exposure on postoperative opioid use in patients receiving cryoneurolysis. Fourth, the use of a single site and surgeon allowed for excellent control over implementation of the multimodal pain protocol and surgical technique; however, this also limits the generalizability of findings. Fifth, pain data were not available to compare groups after discharge. Nonetheless, given that patients in the cryoneurolysis group showed improved functional outcomes and were prescribed significantly fewer cumulative opioids than patients in the control group, it is reasonable to assume that pain intensity in the cryoneurolysis group was not higher than that in the control group. Sixth, because this was a retrospective study with historical controls, other confounding factors could have influenced study outcomes. However, potentially confounding variables (ie, BMI, prior opioid exposure, age, and ASA physical status classification) were included in the multivariable regression model to optimize comparison of the 2 groups. Last, cost-effectiveness was not assessed in this study, which would benefit from further assessment in a separate study. Finally, data pertaining to health-care costs were not included in this study. Despite a prior study suggesting that opioid prescriptions are associated with increased health-care costs [23], further study is warranted to determine if cryoneurolysis results in potential cost-savings for patients.

Conclusions

This retrospective study suggests that, when added to a multimodal TKA pain protocol, preoperative cryoneurolysis provides superior pain control and allows patients to take fewer opioids during hospitalization and during the 6-week recovery period than a multimodal TKA pain protocol alone. Optimization of pain control in the perioperative period is associated with reduced hospital LOS, a decreased rate of readmission, fewer postoperative complications, and improved patient satisfaction with surgery [1]. Achieving good pain control during the initial postoperative period is also critical to avoiding the development of chronic pain and long-term opioid use. Novel pain management modalities that can allow patients to recover from painful surgery with fewer opioids are critical to achieve the nationwide goal of reducing opioid prescribing without compromising quality of care.

Conflicts of interest

The authors declare the following financial interests and personal relationships which may be considered as potential competing interests: J. A. Urban has received speaking fees, consulting fees, and research funding from and holds stock options in Pacira BioSciences, Inc. K. Dolesh is a paid consultant for Pacira BioSciences, Inc. E. Martin has nothing to disclose.

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