Perioperative & Critical Care: Research

Evolution of Pain Control for Adult Pectus Excavatum Repair

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ABSTRACT

BACKGROUND Pain control after minimally invasive repair of pectus excavatum (MIRPE) can be challenging, especially in adult patients undergoing surgical repair. This study reviewed different analgesic modalities used over ≥10 years after pectus repair.

METHODS A retrospective analysis was performed of adult patients (≥18 years) who underwent uncomplicated primary MIRPE at a single institution from October 2010 to December 2021. Patients were classified by analgesic modality used: epidural, elastomeric continuous infusion subcutaneous catheters (SC-Caths), and intercostal nerve cryoablation. Comparisons among the 3 groups were performed.

RESULTS In total, 729 patients were included (mean age, 30.9 ± 10.3 years; 67% male; mean Haller index, 4.9 ± 3.0). Patients in the cryoablation group required significantly lower doses of morphine equivalents (P < .001) and had overall the shortest hospital stay (mean, 1.9 ± 1.5 days; P < .001) with <17% staying >2 days (vs epidural at 94% and SC-Cath at 48%; P < .001). The cryoablation group had a lower incidence of ileus and constipation (P < .001) but a higher incidence of pleural effusion requiring thoracentesis (P = .024). Mean pain scores among groups were minor (<3), and differences were insignificant.

CONCLUSIONS The use of cryoablation in conjunction with enhanced recovery pathways provided significant benefit to our patients undergoing MIRPE compared with previous analgesic modalities. These benefits included a decrease in length of hospital stay, a reduction of in-hospital opioid use, and a lower incidence of opioid-related complications associated with constipation and ileus. Further studies to assess additional potential benefits with long-term follow-up after discharge are warranted.

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Pectus excavatum (PE) is the most common congenital chest wall malformation, and surgical repair is indicated for symptomatic patients.^{1,2} The cardiopulmonary benefits of repair have been documented in well-powered studies.³⁻⁶ The "Nuss" or minimally invasive repair of PE (MIRPE) has been the standard of care for adolescents since its introduction in 1997.^{1,7} Although with technique modifications MIRPE has been successfully extended into the adult population, the procedure is more

difficult in adults, and increased complications have been reported.⁸⁻¹⁰

Postoperative pain after MIRPE can be significant, and high doses of opioids may be required. Pain control may be especially challenging in adult patients as a result of greater weight and chest wall rigidity. Pain can also be a significant factor after MIRPE that incites complications and prolonged hospitalizations, which are reported up to 10 days in some adult cohorts.¹¹⁻¹³ With the current opioid epidemic in the United States, postoperative pain

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modalities that reduce postoperative pain, associated complications, and hospital stay should be prioritized, as well as those modalities that minimize quantity and duration of opioid use.¹⁴ This study reviews the outcomes of 3 different pain management regimens for postoperative pain control after over a decade PE repair, including an enhanced recovery pathway protocol.

PATIENTS AND METHODS

A retrospective review of consecutive adult patients (>18 years) who underwent PE repair by a single surgeon (D.E.J.) at the Mavo Clinic Hospital, Arizona from January 1, 2010 to December 31, 2021, was performed. The Mayo Clinic Institutional Review Board approved this study. Patients undergoing primary MIRPE repairs were included in the comparison cohorts. Those patients with previous repair at another institution who were undergoing a revision PE procedure, open procedures, or hybrid procedures or who had other concurrent surgical procedures were excluded because of the extensive differences in procedure times, associated pain, and length of hospitalization. Patients with a history of chronic pain requiring previous narcotic use were additionally excluded. Patients who experienced fractures during repair, who required sternotomy, or who had other significant postoperative complications that affected length of stay and were unrelated to pain or pain medication use were also excluded. Patients were classified into 3 groups according to analgesic modality: epidural, elastomeric continuous infusion subcutaneous catheters (SC-Caths), and intercostal nerve cryoablation (Cryo). Given the potential baseline differences among the 3 groups, a prespecified matched analysis on the basis of age and sex was also run for statistical comparison.

SURGICAL TECHNIQUE FOR PRIMARY CASES. All patients with primary cases underwent a thoracoscopically modified MIRPE with insertion of at least 2 bars. Our surgical technique has been previously described.⁹ A modification of the technique in 2016 added a "hammock" tie in the intercostal space and the sternum.9 A chest tube was left in all patients and removed when the output was <350 mL in 24 hours. Criteria for discharge included adequate pain management (pain score \leq 4) with oral pain medications and without substantial cognitive or respiratory adverse effects. Discharge was delayed if administration of intravenous narcotics or increasing dosage of opioids was required. Discharge was also delayed for postoperative complications, such as ileus, nausea and vomiting, continued high or bloody chest tube output, or other medical issues.

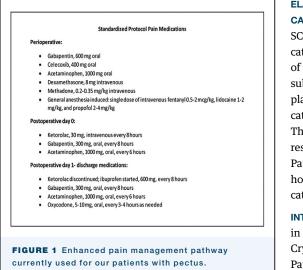
Patients were followed up after discharge at 1 to 2 weeks, 6 weeks, 6 months, and annually. Those patients who did not reside locally were followed up by telephone or video and sent surveillance imaging unless an issue or complication occurred. Long-term follow-up information was collected both by clinical follow-up of chart abstraction of documentation occurring during inperson, telephone, or written communication on the date of the visit and during standardized chest imaging follow-up of implants, which included an associated retrospective survey that required patients to recall information on the use of pain medication during that time period and information about current pain. Followup documentation was more frequent in the latter half of the study, so more information was collected from patients having SC-Cath and Cryo. Bar removal generally occurred at 3 to 3.5 years.

Study end points included hospital morphine equivalent use, length of hospitalization, and 30-day postoperative complications, especially as related to pain and pain medication use. In-hospital postoperative pain scores comprised a secondary end point. Our protocol goal for pain control was to maintain a pain score less than 4. Patients rated their postsurgical pain on a visual analogue scale (0 [no pain] to 10 [worst pain]) every 15 minutes in the recovery room and at least every 4 hours during their hospitalization. Because most patients remain hospitalized for <4 days, comparisons among modalities were made only for the first 3 days. For pain score comparison among groups, mild pain was defined as a daily pain score mean of \leq 3, whereas a score of 4 to 6 corresponded to moderate pain, and scores >7 corresponded to severe pain.¹⁵ After hospital discharge, pain scores were collected at postoperative visits by written or verbal communication with the patients. Patient data were obtained by reviewing the patient's electronic health record. Electronic medical records were changed at the hospital from partial paper or electronic Cerner to all electronic Epic records in October of 2018, and records before the use of Epic had missing medication records that led to exclusion of some epidural-treated patients for missing data. Enhanced recovery pathway medications are reviewed in Figure 1.

EPIDURAL COHORT. Beginning in October 2010, the thoracic epidural modality was used for pain control. The catheter was placed though a midline or paramedian approach at the T5-T6 or T6-T7 interspace. Infusion with fentanyl and a local anesthetic agent was initiated intraoperatively. Beginning in November 2010, in response to issues arising from both narcosis and poor pain control, the decision was made to remove the opioid content and use only the local anesthetic infusion in the epidural modality. This approach was

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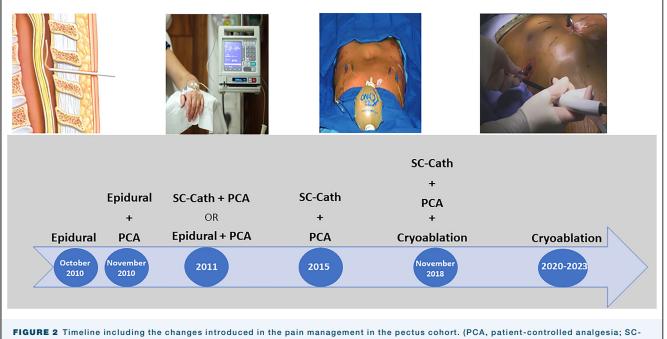
combined with postoperative intravenous patientcontrolled analgesia (PCA) with fentanyl or hydromorphone. Epidural catheters were left in place until pain was controlled, with a transition to oral medications, or unless there were complications with the epidural catheter that required early removal.

Starting in 2011, the first SC-Caths were placed, and patients were given a choice of their pain control modality. By 2014, epidural catheters were rarely requested by patients, and beginning in 2015, SC-Caths were solely used (Figure 2).¹⁶

ELASTOMERIC CONTINUOUS INFUSION SUBCUTANEOUS

CATHETERS. For patients receiving treatment with the SC-Cath, On-Q (Avanos Medical), 7.5-cm wound catheters were inserted bilaterally at the completion of the procedure. The catheters were inserted subcutaneously through tunnelers in a superficial plane lateral to the surgical site (Figure 3). Each catheter infused ropivacaine, 0.2% locked at 7 mL/h. The catheters were attached to a 750-mL, fill-volume reservoir and remained for a maximum of 7 days. Patients were discharged home with an additional 48 hours of infusion unless they asked to have the catheter removed.

INTERCOSTAL NERVE CRYOABLATION. Cryo was initiated in November 2018, with patients having a choice to have Cryo as an additional therapy to the SC-Cath vs not. Patients additionally had PCA available in the immediate postoperative period. Patients with both SC-Caths and Cryo were included in the Cryo cohort for comparisons. As of January 1, 2020, the use of SC-Caths and PCA was discontinued in patients receiving Cryo. For Cryo, a CryoICE Cryo2 cryoablation probe (Atricure) was applied at -60° C for 120 seconds from the third to the eighth or ninth intercostal nerves bilaterally (depending on the number of bars placed and the location of the bars or chest tube). The probe was introduced through the pocket incisions and the intercostal space, applied directly to the intrathoracic nerve (Figure 4). Single-lung isolation was used to gain access to the side undergoing ablation. An intercostal



Cath, elastomeric continuous infusion subcutaneous catheter.)

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FIGURE 3 On-Q catheters (Avanos Medical) inserted subcutaneously in a plane superficial to the rib.

block with 60 mL of 0.25% bupivacaine and 10 mg of dexamethasone was also performed bilaterally.

STATISTICAL ANALYSES. Comparisons among 3 groups were performed using analysis of variance or the Kruskal-Wallis test (according to variables distribution) or χ^2 for categoric variables. Continuous data are reported as mean \pm SD or median (interquartile range) according to distribution, and categoric variable are reported as count (percentage). Significance was defined at .05.

RESULTS. In total, 729 patients underwent an uncomplicated primary MIRPE during the study period. Table 1 reviews the demographics and outcomes of the patients. Patients undergoing Cryo required significantly lower morphine equivalents and had the shortest hospital stay (Table 1, Figures 5 and 6). Overall pain scores were in the mild category (<3) for most of the patients, with no significant differences among categories (Figure 7). The Cryo group also had a lower incidence of complications related to constipation and ileus; however, these patients experienced a higher incidence of pleural effusions requiring thoracentesis



FIGURE 4 Cryoablation probe introduced through the pocket incisions.

(Table 1). Groups were not equally matched; therefore, a smaller cohort of equally matched patient groups was also compared. Findings remained consistent in this analysis and are included in Table 2.

Regarding long-term follow-up from the Cryo group, 56.9% of patients reported needing no further narcotics within the first 1 to 2 weeks postoperatively vs 24.0% of SC-Cath patients (P < .001). There was an overall trend toward less narcotic use in the Cryo group vs the SC-Cath group at 6 months (2.5% vs 5.3%; P = .132) and at 12 months of follow-up (1.5% vs 4.1%; P = .106). At the time of bar removal, a survey was performed of patients assessing their current level of pain, with overall 89.9% reporting no significant pain with the bars in place, with no differences among the groups (epidural, 89.5%; SC-Cath, 89.9%; and Cryo, 89.8%; P = .993). The remaining patients noted some level of pain requiring intervention with, 5.5% using nonsteroidal antiinflammatory drugs or acetaminophen, 1.9% using gabapentin, 1.1% using narcotics, and 1.6% involving the intervention of a pain management physician. There was a high incidence of preoperative anxiety (40.1%), depression (22.8%), and previous chronic pain issues unrelated to their chest (38.6%) in the patient group experiencing chronic pain at the time of bar removal.

COMMENT

Managing postoperative pain after PE repair can be challenging, especially in older patients after MIRPE.9 High opioid use and prolonged pain may delay hospital discharge and increase the risks of complications and readmission.¹⁶⁻¹⁸ Postoperative pain issues have been used by critics of MIRPE to support the argument to use the Ravitch procedure, and many patients have settled for the procedure out of fears of this potential pain.¹⁹ Ideally, adopting superior methods for pain control would offer the greatest patient benefit independent of the type of repair. Initiation of multimodal pharmacology is a significant benefit. This approach has included the use of intraoperative methadone as a preemptive µ receptor blocker, γ-aminobutyric acid analogue or pregabalin, acetaminophen, and nonsteroidal antiinflammatory drug polypharmacy.20 An enhanced recovery protocol (Figure 1) was initiated along with the analgesic modalities, and this protocol likely contributed significantly to pain management strategies and outcomes.

Thoracic epidural analgesia has been a standard method for pain management in thoracic procedures and PE repair for many years.^{18,21} Epidural analgesia was used for postoperative pain control in our early MIRPE experience. Within several years, SC-Caths with PCA were incorporated into the practice. Our randomized study evaluating epidural vs SC-Cath pain management

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TABLE 1 Demographics and Outcomes of Included Patients With 3 Analgesic Modalities: Epidural, Subcutaneous Catheters, and Cryoablation

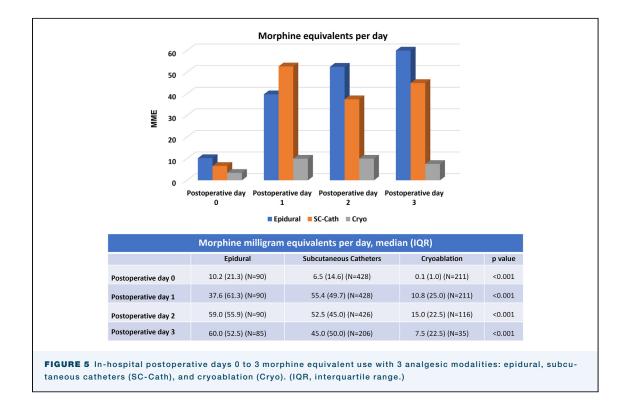
Demographics and Outcomes	Epidural (n = 90)	Subcutaneous Catheters (n = 428)	Cryoablation (n = 211)	P Value
Sex				.027
Male	68 (75.6)	293 (68.5)	128 (60.7)	
Female	22 (24.4)	135 (31.5)	83 (39.3)	
Age, y, mean ± SD	33.3 ± 11.0	31.2 ± 10.0	29.1 ± 10.5	.002
Haller Index, mean ± SD	4.6 ± 1.7	4.9 ± 3.0	4.9 ± 3.6	.668
Bars used				<.001
2	54 (60.0)	296 (69.2)	106 (50.2)	
3	36 (40.0)	132 (30.8)	105 (49.8)	
Duration of surgery, min, mean ± SD	149 ± 50.6	157.9 ± 60.2	155.7 ± 45.1	.456
Length of hospital stay, d, mean ± SD	4.2 ± 1.2	2.8 ± 1.2	1.9 ± 1.5	<.001
Length of hospital stay >2 d	85 (94.4)	206 (48.1)	35 (16.6)	<.001
30-d complications				
Pleural effusion requiring thoracentesis	5 (5.5)	19 (4.4)	21 (9.9)	.024
Right side	4 (80.0)	8 (42.1)	13 (61.9)	
Left side	0 (0.0)	5 (26.3)	2 (9.5)	
Bilateral	1 (20.0)	6 (31.6)	6 (28.6)	
Bleeding requiring intervention	1 (1.1)	4 (0.9)	2 (0.9)	.988
Significant constipation	23 (25.6)	105 (25.5)	11 (5.2)	<.001
Constipation requiring ED visit	9 (9.0)	9 (2.1)	4 (1.9)	<.001
lleus requiring ED visit	5 (5.6)	5 (1.2)	0 (0.0)	<.001
ED visit for uncontrolled pain	2 (2.2)	22 (5.1)	4 (1.9)	.094
Pneumothorax requiring tube placement	1 (1.1)	4 (0.9)	2 (0.9)	.577
Vomiting	5 (5.6)	33 (7.7)	9 (4.3)	.238
Pneumonia confirmed by culture	0 (0.0)	3 (0.7)	1 (0.5)	.706
Pulmonary embolism	1 (1.1)	1 (0.2)	0 (0.0)	.354
Delirium	0 (0.0)	4 (0.9)	0 (0.0)	.564
Infection (confirmed by culture)	0 (0.0)	8 (1.9)	5 (2.4)	.354
Superficial	0 (0.0)	6 (1.4)	3 (1.4)	.526
Deep	0 (0.0)	2 (0.4)	2 (0.9)	.556

after PE repair was published and noted no significant advantage to either modality (hospital stay 3.5 days vs 3.3 days)¹⁶; however, patient preferences ultimately led to SC-Cath as the sole pain management modality until Cryo was introduced in late 2018. Although the hospital length of stay was reasonable, patients were still requiring significant quantities of opioids to control pain.¹⁶ Initially, both SC-Caths and PCA were continued along with Cryo in response to published reports of an initial 24-hour refractory pain period.²² This approach proved unnecessary, and the SC-Caths and PCA were discontinued.

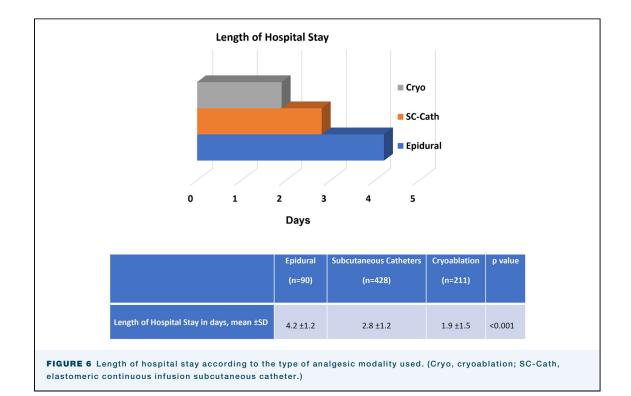
Morphine equivalents were slightly higher on postoperative day 1 when the SC-Caths and PCA were being used (Figure 5). This finding was hypothesized to be secondary to the availability of the opioids to the patient with the ability to push the button easily vs having to ask nursing for oral medication. Overall, postoperative day 0 morphine equivalent use was extremely low, and it is likely secondary to the effects of the intraoperative methadone used in addition to the local anesthetic agent injected intraoperatively as an intercostal block. Overall, in-hospital morphine equivalents were significantly lower in the Cryo group compared with all other pain modalities without significant differences in the pain scores (Table 2, Figures 5 and 7). Possibly, PCA availability could have increased opioid use in the other analgesic modalities given their PCA access (SC-Cath, overnight; epidural, 24-48 hours).

Hospital length of stay varied greatly among publications on adult PE repair, with mean durations reported up to 10 days.¹¹⁻¹³ The Cryo cohort had the shortest hospitalization (mean, 1.9 days), with <17% staying more than 2 days vs the epidural (94%) and SC-Cath (48%) cohorts (P < .001). Multiple factors contribute to length of hospitalization, and trends over time have favored a decreased length of stay. These factors, in addition to pain modality, likely included education of nursing, patients, and staff. The cost of the pain modalities is a variable that should be considered; however, it is dependent on hospital contracting. Approximate

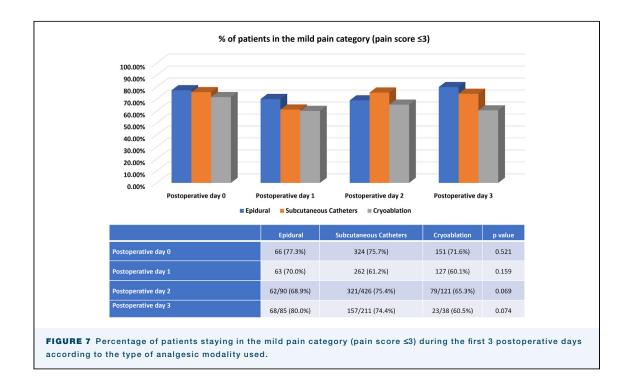
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costs vary, but estimates include the following: Cryo, \$2500 to \$2800, epidural, \$1000 to \$1500, and SC-Cath, \$500 to \$750. However, the savings per day of a hospital stay must also be considered (\$2000-\$4000). Some complications associated with opioid use, including nausea and vomiting, were not significantly different among groups, and this finding may reflect postanesthesia effects and the intraoperative use of



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methadone. There was, however, a lower incidence in the Cryo group of complications associated with ileus and constipation (P < .001), which included emergency department visits in the immediate postoperative discharge period. Other causes for emergency department visits and readmissions were not found to be significantly different apart from significantly higher associated evaluations required for pleural effusions and thoracentesis (P = .024) with Cryo. This result may be subject to missing data because many patients returned to their home state and may not have reported subsequent issues. The higher incidence of pleural effusions with Cryo may be associated with the use of \geq 3 bars vs 2 bars for MIRPE in the Cryo group (49%) vs the epidural (40%) and SC-Cath (30%) groups (P < .001). Although a subanalysis of the Cryo cohort that looked at 2 bars (10.4% pleural effusions) vs >3 bars (11.7% pleural effusions) did not show a significant difference (P = .800). To our knowledge, an increased incidence of pleural effusions with use of Cryo has not been reported; however, both multiple bars and cross bars have been reported to be associated with an increased incidence of effusions.23,24

Regarding long-term follow-up, many of the data were collected retrospectively, along with secondary recall of patients, which may have been subject to considerable bias. Ideally, close follow-up of a patient's postoperative pain medication use after discharge until discontinuance would have been performed; however, most patients were from out of town, and after initial discharge follow-up, patients returned home and were followed up by their local providers. Although patients were surveyed about the timing and quantity of their narcotic use after they were discharged from the hospital, some answers were incomplete or were marked as "unsure"; therefore, these patient outcomes are unable to be accessed. Patients with epidural and SC-Cath modalities were discharged home on both long-acting time-release morphine and oxycodone, whereas patients with Cryo treatment were discharged requiring only tramadol or oxycodone in significantly lesser amounts. Unlike the SC-Cath and epidural groups, more than one-half of the patients in the Cryo group reported no need for narcotics after 1 to 2 weeks postoperatively, with favorable outcomes at 6- and 12-month intervals. Although neuropathic pain is a possibility with Cryo, it would be difficult to distinguish it from intercostal nerve pain secondary to the bars. The expected time for neuropathic pain to emerge is approximately 8 weeks. There was an overall trend toward less narcotic use in the Cryo group vs the SC-Cath group at 6 months (2.5% vs 5.3%; P = .132) and 12 months of follow-up (1.5% vs 4.1%; *P* = .106).

This study has the limitations of a retrospective study with all the inherent biases. The surgical technique was modified to some degree during the study period, and the experience of the surgeon improved with time, a factor likely reflected in the relatively stable surgical procedure time despite the addition of Cryo, which increases operative time to perform. There are other factors that may have affected outcomes of hospital stay and opioid use. The results reported are those of a single

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TABLE 2 Demographics, Surgery Information, Hospitalization, and Postoperative Pain of Matched Cohort Patients Undergoing Minimally Invasive Repair of Pectus Excavatum With Epidural vs Subcutaneous Catheter vs Cryoablation Modalities

Variables	Epidural (n = 50)	Subcutaneous Catheters (n = 50)	Cryoablation $(n = 50)$	P Value
Age, y, mean ± SD	32.0 ± 9.1	33.7 ± 9.3	32.8 ± 10.4	.682
Sex				1.000
Male	37 (74.0)	37 (74.0)	37 (74.0)	
Female	13 (26.0)	13 (26.0)	13 (26.0)	
Duration of surgery, min, mean ± SD	160.9 ± 45.6	166.5 ± 78.2	155.6 ± 39.6	.630
Length of hospital stay, d mean ± SD	3.7 ± 1.0	2.6 ± 0.9	2.2 ± 2.4	<.001
Length of hospital stay >2 d	45 (90.0)	22 (44.0)	10 (20.0)	<.001
Morphine milligram equivalents/d, median (IQR)				
Postoperative day 0	80.2 (32.1)	80.1 (29.2)	63.5 (86.3)	<.001
Postoperative day 1	44.0 (54.0)	60.0 (39.2)	6.5 (27.9)	<.001
Postoperative day 2	65.0 (64)	52.5 (41.0)	12.5 (27.0)	<.001
Postoperative day 3	60.0 (53.0)	41.3 (43.0)	5.0 (47.0)	.009
Bars used				.310
2	27 (54.0)	33 (66.0)	26 (52.0)	
3	23 (46.0)	17 (34.0)	24 (48.0)	
30-d complications				
Pleural effusion requiring thoracentesis	0 (0.0)	2 (4.0)	7 (14.0)	.010
Bleeding requiring intervention	0 (0.0)	0 (0.0)	0 (0.0)	1.000
Significant constipation	12 (24.0)	13 (26.0)	2 (4.0)	.007
Constipation requiring ED visit	5 (10.0)	1 (2.0)	1 (2.0)	.091
Ileus requiring ED visit	2 (4)	0 (0.0)	0 (0.0)	.132
ED visit for uncontrolled pain	2 (4.0)	2 (4.0)	1 (2.0)	.813
Pain score (mild pain category)				
Postoperative day 0	40 (80.0)	39 (78.0)	39 (78.0)	.961
Postoperative day 1	37 (74.0)	41 (82.0)	35 (70.0)	.366
Postoperative day 2	43 (86.0)	43 (86.0)	19/28 (68.0)	.087
Postoperative day 3	40/45 (89.0)	20/22 (91.0)	7/8 (88.0)	.954

Values are n (%) unless designated mean ± SD or median (IQR). ED, emergency department; IQR, interquartile range.

institution and surgeon and may not be reproducible by other investigators.

In conclusion, the use of Cryo in conjunction with enhanced recovery pathways provided significant benefit to our patients undergoing MIRPE compared with previous analgesic modalities. These benefits included a significant reduction of in-hospital use of opioids, a decrease in the length of hospital stay, and a lower incidence of complications associated with constipation and ileus. Further investigations of the longterm benefits, including potential reduction of chronic pain issues, are warranted.

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DISCLOSURES

Dawn E. Jaroszewski reports a relationship with Zimmer Biomet Holdings Inc that includes consulting or advisory and equity or stocks; has patent PectusBlu NexGen with royalties paid to B151018; and is a consultant for and has IP/royalty rights under Mayo Clinic Ventures with Zimmer Biomet, Inc. All other authors declare that they have no conflicts of interest.

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