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Abstract

Introduction: Pectus Excavatum (PEX) is the most common anterior chest wall deformity. While minimally invasive repair of pectus excavatum (MIRPE) has improved perioperative outcomes, there continue to be opportunities to optimize postoperative pain management and reduce length of stay (LOS). We compared the impact of a multimodal expedited protocol utilizing a combination of systemic and regional analgesia (with single shot paravertebral truncal blocks), along with coping techniques (such as meditation), and physical therapy, with systemic analgesia on LOS and opioid requirements.

Methods: 51 patients underwent MIRPE with an expedited recovery protocol in comparison with 112 historical control patients at a single center over 18 years. LOS and opioid analgesic morphine milliequivalent (MME) were compared. Data were stratified for age, biological sex, and Haller index (HI) to identify potential confounding variables.

Results: There was no difference in age or HI between cohorts. LOS was reduced by 59.1% in the enhanced recovery group compared to the historic group (1.8 days vs 4.4 days, SD=0.5664 and 0.9503 respectively, $P< 0.0001$). On postoperative day (POD)1, the expedited patients required an average of 100.7 MME (IQR 61.65-124.3) compared to 123.6 MME (IQR 79.5-161.1) for historic control patients ($P=0.04$). Cumulative MME for POD0-2 was 34.8% less in the expedited recovery patients ($P=$

Conclusions: This MIRPE expedited recovery pain protocol using a standardized multimodal analgesia strategy and regional anesthesia is a safe and effective therapeutic plan that results in decreased opioid analgesic requirements and a significantly decreased LOS.

Keywords

Nuss repair, pain management, enhanced recovery, pectus excavatum

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Abstract

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Conclusions: This MIRPE expedited recovery pain protocol using a standardized multimodal analgesia strategy and regional anesthesia is a safe and effective therapeutic plan that results in decreased opioid analgesic requirements and a significantly decreased LOS.

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Level of Evidence rating: therapeutic

Introduction

PEX is the most common deformity of the anterior chest wall. It may be present at birth or develop during childhood, typically worsening with continued growth. Patients often present with exertional dyspnea, chest pain, and a poor body image. Repair is typically done between 10 – 15 years.[1] The Nuss procedure was introduced in 1989 as an innovative approach to the repair of PEX. The Nuss procedure has replaced the Ravitch procedure as the most commonly performed repair for PEX. Positive outcomes can be expected in 95-98% of cases.[1-3] In comparison to the Ravitch repair, the Nuss repair has been shown to have increased postoperative pain and a higher opioid requirement, especially in older patients.[4-5] There is evidence that the minimally invasive approach has been shown to increaseLOS.6 The average LOS following a Nuss minimally invasive repair is 5 days in the U.S. and 7 days in Europe.[6-7] After discharge, opioid medications have been reported as being required for as long as 1.5 months status post Nuss repair.[8]

Challenges associated with postoperative pain management have prompted some to question if surgical intervention for PEX is worth the pain associated with the procedures.[9] Strategies employed to address pain management that have been reliant on opioid analgesics have not demonstrated sufficient gains in LOS and pain control. The current opioid crisis demands innovative approaches to decrease opioid use.

Many analgesic approaches have been investigated to improve postoperative pain control and decrease LOS after Nuss repair. Thoracic epidural analgesia employed for MIRPE has been described to increase LOS without improvement in pain control as compared to patient controlled analgesia (PCA).[10] Cryotherapy has emerged for post operative pain control demonstrating a shortened LOS (2-3.9 days) and improved pain control as compared to alternative methods (most commonly compared to epidural analgesia).[11-21]

There have been multiple reports of the efficacy of paravertebral nerve blocks in pediatric perioperative pain management, particularly in thoracic and abdominal cases.[22-25] There has been limited investigation regarding the use of paravertebral blocks in PEX-corrective procedures.[26-27] Similarly, intercostal nerve blocks have shown some potential for improved post-Nuss pain control, with less opioid use in the first 24 postoperative hours as compared to PCA.[28]

Non-pharmacotherapeutic techniques for pain control have been demonstrated in the literature to improve analgesia. Self-hypnosis training has been associated with use of fewer morphine equivalents after Nuss repair in conjunction with thoracic epidural, as well as a shorter LOS.[29] Cognitive behavioral therapy has also shown preliminary evidence for utility in managing postsurgical pain.[30] In the orthopedic literature, preoperative mindfulness training has been found to aid in controlling pain intensity and psychological stress.[31-32] One study using these holistic techniques demonstrated success in achieving consistent POD1 discharge after Nuss repair with adequate pain control.[33]

Attempts to standardize postoperative Nuss care to enhance pain control and expedite discharge have met with varying impact on opioid pain medication use and LOS compared to their control groups.[34-37] While the demonstrated improvements in MME usage and LOS made by these proposed Enhanced Recovery After Surgery (ERAS) protocols may be an improvement compared to their respective internal study control cohorts, their LOS is comparable to what has been documented in literature for non-ERAS protocols.[10-21, 26-29] In many of these studies , the pain management approach to decreased LOS is often focused on a single variable, typically cryoablation, epidural, or PCA.

We propose a multimodal analgesia protocol for postoperative pain management that reduces LOS and postoperative inpatient opioid requirements. This protocol incorporates a standardized approach starting at the preoperative visit, through the perioperative course, to the postoperative

visit. This protocol includes perioperative blocks, multimodal analgesia medications, mindfulness and distractive coaching from Child Life (CL) specialists, and strong support from physical therapy.

Methods

Retrospective and Prospective Chart Review (Table 1)

Ethics and Institutional Review Board (IRB) approval was obtained (#0199-18-EP). A retrospective chart review for patients with pectus excavatum who had undergone Nuss repair between the ages of 10 and 19, managed at Children's Hospital and Medical Center, Omaha, Nebraska (Table 1). Prospective data collection for the expedited recovery protocol was performed using EPIC data extraction after study consent was obtained from caregiver and/or patient. Dates of operation were between 3/2003 to 12/2020. Data included standard demographics (age, sex, weight, cardiopulmonary comorbidities), as well as elements contributing to PEX (Haller index, symptomatology), surgical hospital admission factors (number of bars, length of operation, analgesic approach, morphine milliequivalent consumption, length of stay). Exclusion criteria included comorbid conditions in which protocol medications were contraindicated. Primary outcomes measures were LOS and opioid MME required until discharge. Two patients were excluded from the study: one who had a single kidney and was not given nonsteroidal anti-inflammatory drugs, and another who had a breast reduction concurrently with the Nuss repair.

MME Calculation

A subset of patients with complete medication administration records logged in the electronic medical record system were surveyed for perioperative opioid pain medication use (control n=49, expedited protocol n=51). 49 of the 112 historic control patients were found to have sufficiently complete medication records to be included in this subset. Opioid medications were tabulated and converted to oral MME via standardized conversion calculators.38-42

Statistical Analysis

Statistical analysis was completed using GraphPad Prism 9. Descriptive statistics, t-test, and ANOVA or their non-parametric counterparts were utilized where appropriate. A $P < 0.05$ was used to establish significance. Median age of study participants was used for age stratification cutoffs. Median Haller index was used for analyses stratified by Haller index.

Expedited Discharge Protocol (Table 2)

Preoperative Education:

The preoperative clinic appointment was used to orient the patient and family to the planned protocol, including mindfulness and relaxation techniques instructed by our institution's CL program. Significant time during the visit is dedicated to explaining the procedure, and setting post operative expectations for the patient and family, with a focus on cultivating a relationship amongst surgeon, patient, family, and CL. The patient's coping mechanisms, anxiety, and pre-existing pain issues are assessed by CL who then implement auxiliary pain control strategies, such as mindfulness and relaxation techniques.

Preoperative Period

Consent for study participation was obtained the day of operation. CL met with the patient and family again to remind them of non-pharmacological techniques. Premedication included a loading dose of 200 mg gabapentin.

Intraoperative Period

After general anesthesia induction, bilateral paravertebral nerve blocks were placed under ultrasound guidance using ropivacaine or bupivacaine (max dose 2.5 mg/kg) divided between T4, T6, and T8 levels (smaller volume in T4 blocks). Intravenous (IV) acetaminophen (15mg/kg, max 1g) and 15mg IV ketorolac were given at closure, with IV hydromorphone titrated prior to emergence and extubation as needed.

Postoperative Period

In the post-anesthesia care unit, patients were given 200mg gabapentin by mouth, 5mg diazepam by mouth, and a morphine or hydromorphone patient-controlled analgesia was initiated, including a basal infusion

Table 1. Demographics. Demographics of historic and expedited protocol groups. Median used for data subsets with non-normal distribution. Historic Protocol N=112. Expedited Protocol N=51.

	Historic Protocol	Expedited Protocol	P
Mean Age	15.5	16	0.0849
Median Weight	56.4	58.2	0.8759
Median Haller Index	4.3	4.5	0.7049
Biological Sex	Male 85.7% Female 14.3%	Male 80.4% Female 19.6%	0.4891
Median Number of Bars	1	2	<0.0001

Table 2. Nuss Repair Expedited Protocol Outline. Nuss repair expedited discharge protocol outline, detailing elements contributing to pain control in the pre-, intra- and post-operative settings. See methods section for full medication details.

Preoperative Clinic Visit	Immediate Preoperative Period	Immediate Postoperative Period	Inpatient Regimen	Outpatient Regimen
Child Life auxiliary techniques	Child Life visit	200 mg gabapentin	Child Life visits PRN	Continue auxiliary techniques
Detailed operative planning/ relationship building	200 mg gabapentin		PCA → transition to oral analgesia: • Naproxen 250 mg BID • Acetaminophen 500 mg q 6 hrs • Oxycodone 0.5-1 mg/kg (max dose 10 mg) q 4-6 hrs • Gabapentin 200 mg TID • 0.05-0.1 mg/kg diazepam (max dose 5 mg) q 6 hrs prn	• Naproxen 250 mg BID • Acetaminophen 500 mg q 6 hrs • Oxycodone 5 mg q 4-6 hrs • Gabapentin 200 mg TID x 14 days • 3-5 mg diazepam prn only if used inpatient
Assessment of coping mechanisms/ anxiety	T4, T6, T8 bilateral paravertebral nerve block (intra-op phase)		0.05-0.1 mg nalbuphine as needed for urinary retention Bowel regimen of polyethylene glycol 3350 daily, 100 mg docusate daily Antiemetics as needed	Continue inpatient bowel regimen

and demand dosing for breakthrough pain. Intravenous ketorolac was scheduled every 6 hours alternating with 15 mg/kg intravenous acetaminophen every 6 hours (max 812.5 mg/dose, total max 3250 mg in 24 hours), 5 mg of oral diazepam every 6 hours as needed, and gabapentin was continued three times a day. Side effect management included ondansetron IV as needed, a bowel regimen, and any opioid induced urinary retention was treated with 0.05-0.1mg/kg IV nalbuphine as needed. The basal rate of the PCA was discontinued at midnight the evening of the operation. On POD1, the PCA was discontinued in the morning and all intravenous medications were converted to oral alternatives. These included naproxen 250 mg every 12 hours, acetaminophen 500-750 mg by mouth every 6 hours, oxycodone 0.5-1 mg/kg (max dose 10 mg) every 4-6 hours, gabapentin 200 mg three times daily, and 0.05-0.1 mg/kg oral diazepam (max dose 5 mg) every 6 hours as needed for muscle spasms. Oxycodone 2.5 mg was given every 4 hours as needed for breakthrough pain. CL continued to provide adjunctive pain control and relaxation techniques throughout the admission. Physical therapy was used to aid in ambulation and walking the stairs.

At discharge, patients were provided a regimen of 250 mg naproxen every 12 hours, 500 mg acetaminophen every 6 hours, 5-7.5 mg oxycodone 4 times daily as needed with 2.5 mg dosage as needed for breakthrough pain, 3-5 mg diazepam as needed (only if found useful during inpatient stay), and 200 mg gabapentin three times daily for a total of one week. Bowel regimen remained the same until opioids no longer were required. Patients were instructed to wean the oxycodone as they were able. The gabapentin was prescribed for a total of 7 days postoperatively.

Patients were seen within 2 weeks in clinic for a postoperative assessment, or earlier if pain control issues arose after discharge. At that visit, the naproxen was generally discontinued, and the patient placed on ibuprofen with instructions to wean. They were encouraged to keep utilizing the relaxation techniques taught by CL.

Results

Retrospective data extraction yielded 112 patients in the control (historic protocol) group. This group underwent various analgesic methodologies, including PCAs and epidurals, without a comprehensive multimodal protocol that incorporated non-pharmacological elements. 51 consecutive patients received perioperative pain management according to an early discharge protocol (Table 2), beginning on 5/25/18.

Demographics

Mean age was similar between the historic and expedited protocol groups, at 15.5 and 16 years old, respectively (P=0.0849, Figure 1A). Biological sex makeup of each arm was found to be equivalent, with males making up 85.7% of the historical control cohort, and 80.4% of the expedited protocol group (P=0.4891, Figure 1B, Table 1). Haller index (HI) was similar between the two cohorts, with the historic and expedited protocol groups having median HI of 4.3 and 4.5, respectively (P=0.7049, Figure 1C, Table 1).

LOS

Patients treated under our early discharge protocol had an average LOS of 1.8 days, as compared to historical control patients who received systemic analgesia alone who had an average LOS of 4.4 days (P<0.0001; Figure 2). When stratified to analyze the potential contribution of age, biological sex, and Haller index, none of these variables independently contributed to the duration of LOS.

15.8 years was found to be the average age of all patients, and thus was the threshold used for creating age-based stratification groups to investigate any confounding influence of age on LOS. Internally, no difference was found in the expedited discharge protocol versus the control cohort for LOS when subgroups of patients older and younger than 15.8 years old were compared (P=0.4043 and 0.8362 respectively, Figure 3A). LOS was 4.5 days for historic protocol patients <15.8 versus 4.2 days for historic protocol patients >15.8. LOS was 1.8 days for expedited protocol patients <15.8 versus 1.9 for expedited protocol patients >15.8. A significant decrease in LOS

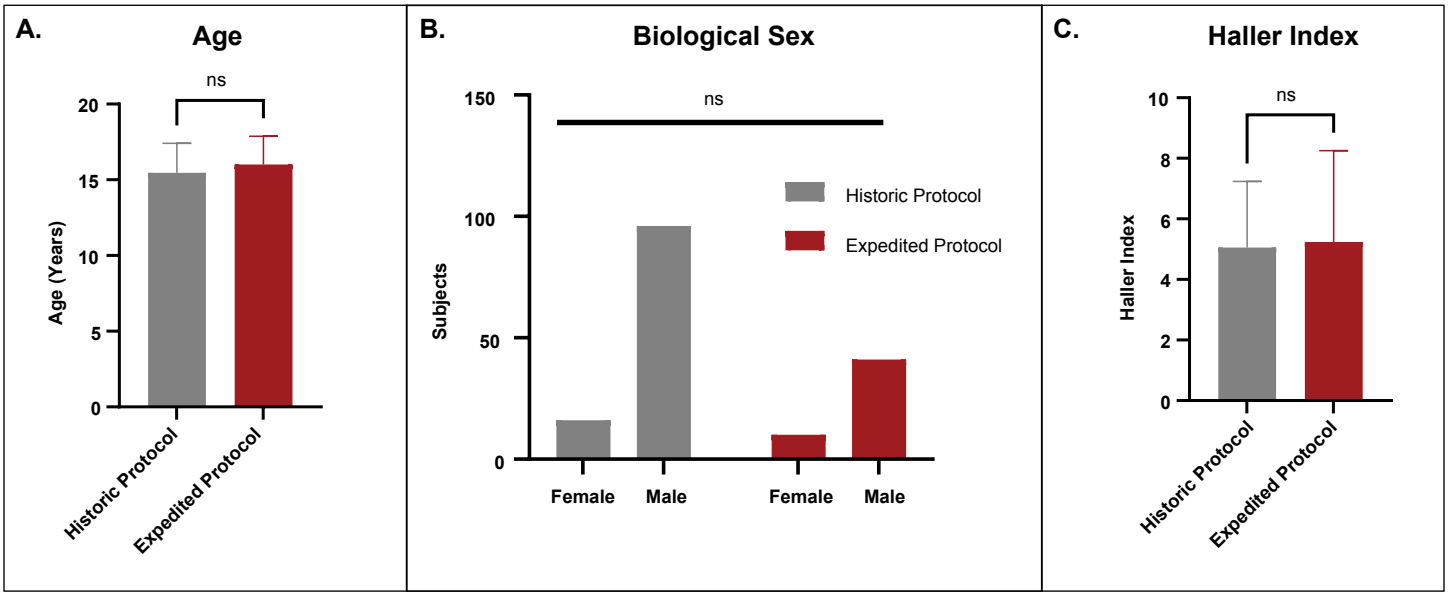

Figure 1. Patient Demographics and Parameters. Patient demographics and pectus deformity severity in the historic and expedited protocol cohorts. A) Mean age for historic and expedited protocol patients was similar, at 15.5 and 16 years old, respectively (P=0.0849). Average age between groups was 15.8 years old. B) Females made up 14.3% of the historic protocol group, and 19.6% of the expedited protocol group respectively. Males accounted for the remaining 85.7% and 80.4% in each corresponding cohort. Biological sex fractionation was equivalent between both cohorts (P =0.4891). C) Median Haller index of the historic protocol group was 4.3, while the Haller index of the expedited protocol group was 4.5 (P =0.7049). Average Haller index between groups was 4.4.

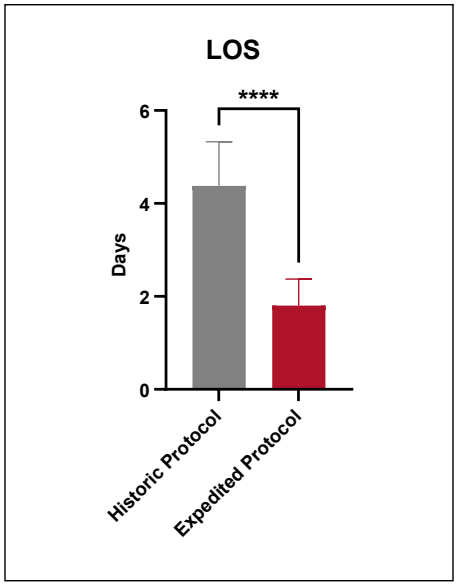

Figure 2. Length of Stay. Total length of stay measured in days for Nuss repair hospital admission. Average LOS for historic protocol patients was 4.4 days, while LOS for expedited protocol patients was 1.8 days (P<0.0001).

was found when each historical subgroup was compared with its expedited discharge protocol counterpart (all P<0.0001, Figure 3A). Age was not internally contributory to the LOS within each treatment group, however each age group was found to have a decreased LOS under the expedited discharge protocol.

Similarly, biological sex was not found to have a significant impact on the LOS between the two groups. Males and females had similar LOS in each treatment group (P=0.6982 and 0.9752 respectively, Figure 3B). LOS was 4.4 days for male historic protocol patients versus 4.5 days for female historic protocol patients. LOS was 1.8 days for both male and female expedited protocol patients. Expedited discharge males and females both had shorter LOS than the same groups in the historical treatment cohort (all P<0.0001, Figure 3B). Biological sex did not significantly impact the internal LOS within the treatment groups, but both males and females were found to have shorter LOS in the expedited discharge group compared to their non-protocol counterparts.

The median Haller index of the two groups was 4.4, which was the value used to separate each treatment cohort into PEX severity subgroups. No difference was found in the LOS within the expedited discharge and historical treatment groups when data was stratified in accordance with PEX severity (P=0.7150 and 0.8996 respectively, Figure 3C). LOS was 4.4 days for historic protocol patients with HI both < and > 4.4. LOS was 1.8 days for expedited protocol patients with HI both < and > 4.4. Expedited discharge patients in each PEX severity group were found to have shorter LOS when matched with their respective historical treatment counterparts (all P<0.0001, Figure 3C). LOS was independent of PEX severity within each cohort, however, expedited discharge patients with both shallower and deeper defects had shorter admissions than non-expedited discharge patients.

Oral MME

Oral MME administration required for adequate pain control was tabulated and compared between the expedited discharge

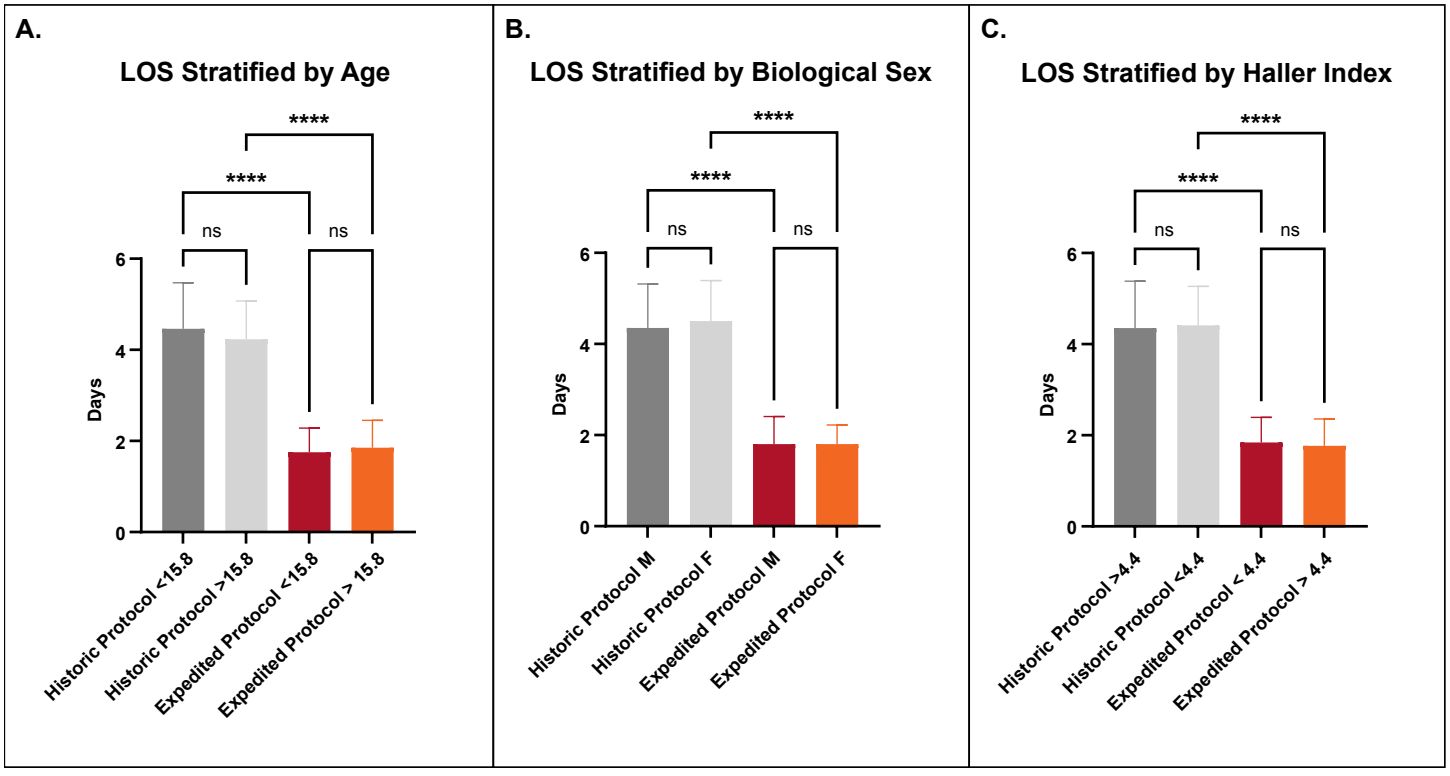

Figure 3. Age, Biological Sex, and Haller Index Contribution to LOS. Stratification of LOS across the variables of age, biological sex, and Haller index. A) 15.8 years old was identified as the average age between both cohorts. Age was not found to be internally different in either experimental group (historic protocol group P=0.4043, expedited protocol group P=0.8362). Differences in LOS between treatment groups persisted between correlating subgroups upon age stratification (age<15.8 years P<0.0001, age>15.8 years P<0.0001). B) Biological sex was not found to be internally different in either experimental group (historic protocol group P=0.6982, expedited protocol group P=0.9752). Differences in LOS between treatment groups persisted between correlating subgroups upon biological sex stratification (male P<0.0001, female P<0.0001). C) 4.4 was found to be the average Haller index of patients between both cohorts. Haller index was not found to be internally different in either experimental group (historic protocol group P=0.7150, expedited protocol group P=0.8996). Differences in LOS between treatment groups persisted between correlating subgroups upon biological sex stratification (Haller index<4.4 P<0.0001, Haller index>4.4 P<0.0001).

and historical treatment groups. Oral MME requirements were equivalent between cohorts for the day of surgery (P=0.2074 Figure 4A). However, by POD 1 expedited discharge cohort patients required significantly less opioid pain medication to achieve adequate pain control (average 100.7 MME versus 123.6 MME, P=0.04; Figure 4A). Overall, total opioid requirements for POD 0-2 were significantly less in the expedited discharge protocol group compared to the historical treatment patients (210.5 versus 283.8 MME, P=0.0009; Figure 4A). This difference persisted when opioid requirements were standardized for patient weight (3.7 versus 5 MME/Kg, P=0.0016; Figure 4B).

Oral MME requirements were then stratified by age. The average age of patients with complete opioid administration record data between both treatment groups was 15.8, which was then used as the cutoff age to investigate if age had a significant contribution as a confounding variable to pain control. Subjects within both the expedited discharge and historical treatment cohorts were divided into younger and older subgroups to assess MME requirements internally within each treatment group. In neither the expedited discharge nor the historical treatment groups was age found to be a significant contributor to opioid use (P=0.6059 and 0.7518 respectively, Figure 5A). Expedited protocol patients still used less MME compared to historic protocol subjects after stratification of the groups into younger and older cohorts (P=0.0165 and 0.0211, Figure 5A). Age was non-contributory to MME required for adequate pain control.

The cohorts were also divided into subgroups by biological sex for further analysis of pain medication use. No difference was observed internally within either the expedited discharge and historical treatment groups when their MME requirements were stratified by biological sex (P=0.4212 and 0.8359 respectively, Figure 5B). While females in both treatment groups were found to have equivalent pain medication use, males were found to use less opioids in the expedited discharge cohort (P=0.4059 and 0.0012 respectively, Figure 5B). Although males did have improved pain control with the early discharge protocol, biological sex did not otherwise influence pain medication consumption within either treatment groups or for the female patients.

Pain medication requirements were also analyzed in relation to PEX using Haller index as a proxy. A Haller index of 4.4 (median between both groups) was used as a cutoff to separate cohorts by PEX severity. The historical and expedited discharge protocol treatment groups were internally found to use equivalent amounts of opioid pain medication regardless of PEX severity (P=0.8894 and 0.8476 respectively, Figure 5C). Historic protocol patients were found to use more opioids when compared with the expedited protocol counterparts after stratification into less and more severe PEX defect subgroups (P=0.0117 and 0.0364 respectively, Figure 5C.) Overall, Haller index severity did not influence oral MME requirements for adequate pain control.

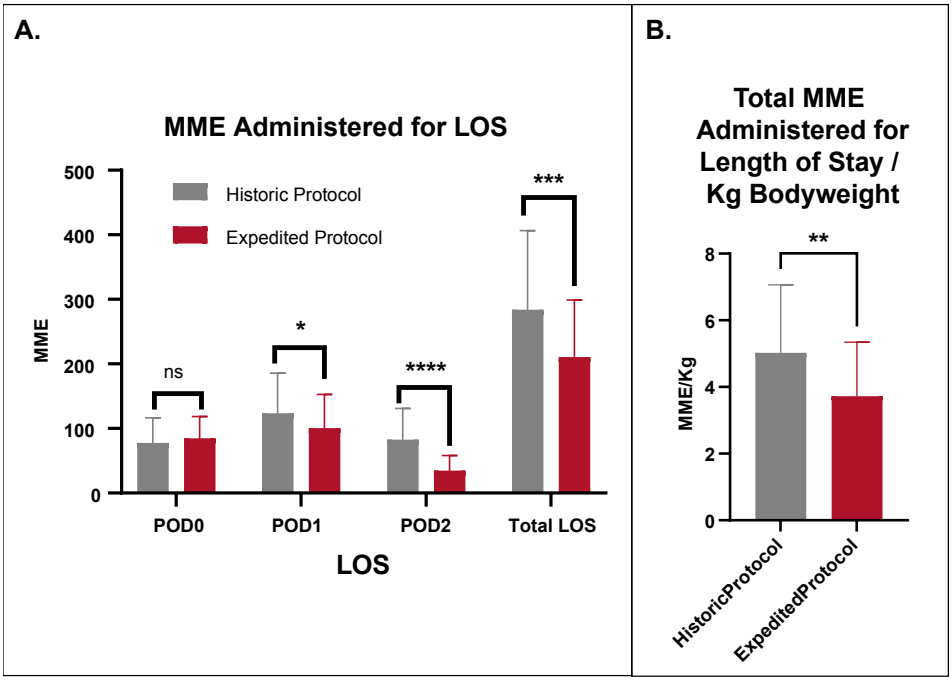

Figure 4. Opioid Pain Medication Administration for Adequate Analgesia. Average oral MME required for adequate pain control. A) Opioid pain medication use was equivalent at the timepoint of POD0 between the groups (POD0 P=2074). At POD1, expedited protocol patients required an average of 100.7 MME to achieve adequate analgesia, as compared to 123.6 MME required by historic protocol patients (P=0.04). Total opioid administration for the entire LOS was less in the expedited protocol cohort (210.5 versus 283.8 MME, P=0.0009). B) This difference remained when drug amount administered was standardized for patient weight (3.7 versus 5 MME/Kg, P=0.0016).

Discussion

The Nuss procedure has become the most commonly used method in the repair of Pectus Excavatum. This approach, while highly successful, is associated with a significant amount of post operative pain leading to extended hospitalization. Multiple approaches have been employed to decrease this increased LOS related to the postoperative pain. This study describes a multimodal approach combining non-pharmacologic coping mechanisms with a standardized multimodal analgesia approach utilizing opioid and non-opioid medications, and regional anesthesia via multi-level single shot paravertebral nerve blocks. This approach to the care of the postoperative Nuss patient demonstrates the potential for POD 1-2 discharge, with a significant reduction in overall LOS.[33, 43] We have shown that improved pain control with LOS is attainable with the utilization of standardized perioperative education and relaxation techniques, coupled with a multimodal analgesia pathway employing resources already at the disposal of patients. Further analysis regarding opioid use after discharge was beyond the scope of this study due to difficulty in obtaining accurate data regarding the precise number of pills remaining from discharge prescriptions at postoperative clinic appointments.

Cryoablation has also shown a decreased LOS, but our model is able to achieve an average LOS of 1.8 days (versus the average 2-3.4 range reported by various studies supporting the use of cryoablation) without the additional costs of increasing operative time and adding another procedure.[11-21] There has also been a report of an increased incidence of bar movement requiring reoperation after cryoablation.[15] When data was stratified for age, older patients who underwent Nuss repair with cryoablation had increased LOS, neuropathic pain, and time

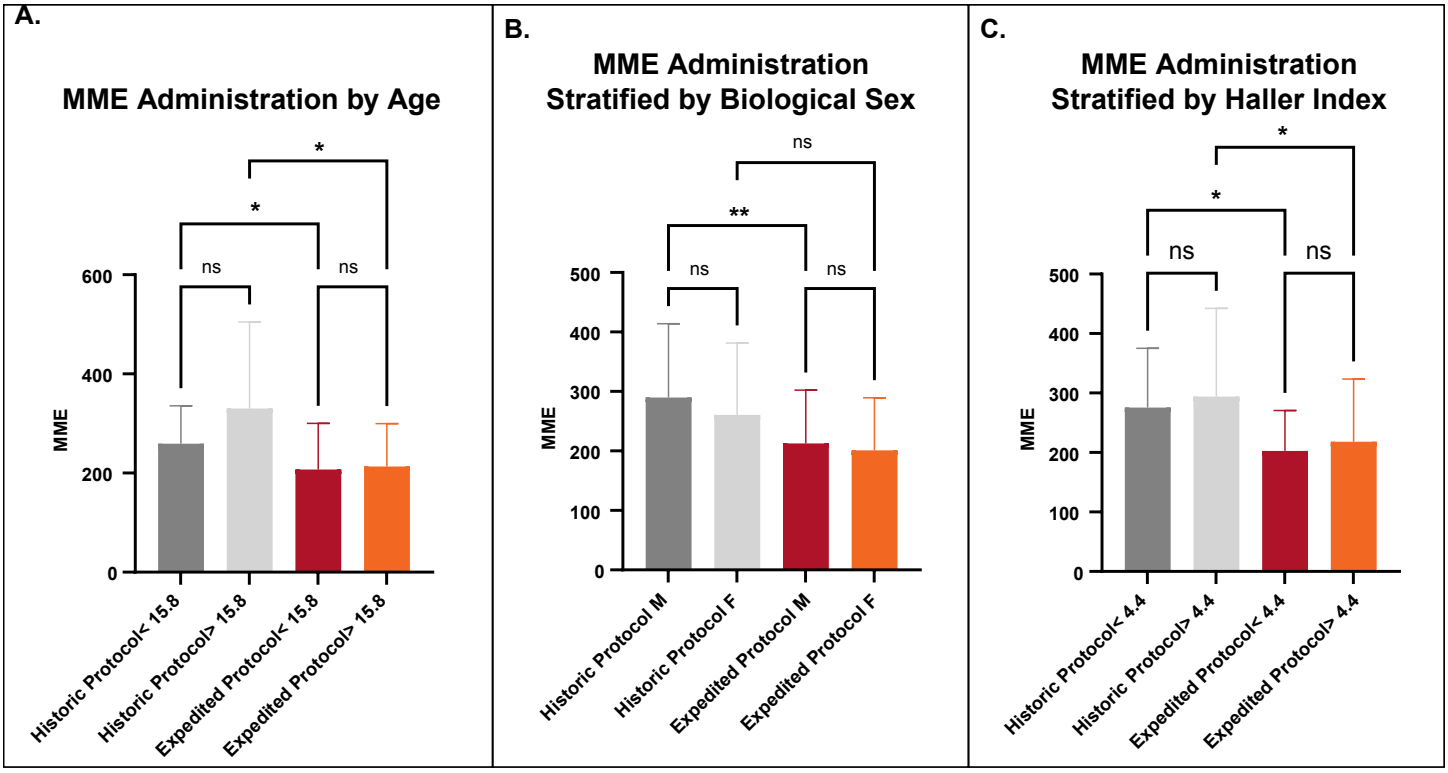

Figure 5. Age, Biological Sex, and Haller Index Contribution to Pain Control. Stratification of oral MME required for adequate pain control across the variables of age, biological sex, and Haller index. A) 15.8 years old was identified as the average age between patients with complete opioid pain medication administration records in both cohorts. Age was not found to be internally different in either experimental group (historic protocol group P=0.6059, expedited protocol group P=0.7518). Differences in overall MME requirements were present between correlating subgroups upon age stratification (age<15.8 years P=0.0165, age> 15.8 years P=0.0211). B) Biological sex was not found to be internally different in either experimental group (historic protocol group P=0.4212, expedited protocol group P=0.8359). Differences in MME requirements between treatment groups persisted for males but not females upon biological sex stratification (male P=0.0012, female P<0.4059). C) 4.4 was found to be the average of median Haller index of patients with complete opioid pain medication administration records between both cohorts. Haller index was not found to be internally different in either experimental group (historic protocol group P=0.8894, expedited protocol group P=0.8476). Differences in overall MME requirements between treatment groups persisted between correlating subgroups upon PEX defect severity stratification (Haller index<4.4 P=0.0117, Haller index>4.4 P=0.0364).

to numbness resolution compared to their younger counterparts.[21]

Prior studies have shown that older patients struggle with more postoperative pain after PEX repair, which can result in longer hospital admissions in those populations.[5,21] Our expedited discharge protocol cohort was found to be effective regardless of age. Importantly, even when stratified for age, both the younger and older subgroups of the expedited discharge protocol exhibited a decreased opioid requirement while achieving adequate pain control and reduced LOS compared to their age-matched controls, speaking to the durability of our model. The fact that our expedited discharge protocol was able to decrease both LOS and oral MME independent of age, biological sex, and Haller index supports that the observations relating to shorter admissions and less opioid use were driven by our comprehensive approach.

The involvement of the Child Life program was a critical component of our protocol. The CL personnel focused on applying their standardized techniques to assess patient's coping mechanisms, which created opportunities for them to offer suggestions for coping mechanisms based on each patient's personalities and hobbies. These techniques included approaches such as games, music, books, music, movies, talk therapy, light activity, meditation, breathing exercises, crafts, and drawing. The patients were also given instructions on the concept of mindfulness to reduce pain and stress anticipation. This encouraged patients to emphasize keeping their attention on the present moment and current focus, rather than their pain, to separate the feeling of anxiety from its potential negative consequences on recovery and pain control.

This expedited discharge protocol demonstrates that a standardized protocol using the combination of regional and systemic pharmacological analgesia combined with perioperative prehabilitation counseling and coping strategies decreases LOS and MME requirements after the Nuss procedure. Implementation of a comprehensive expedited recovery pathway reduces not only length of stay, but also decreases the perioperative opioid analgesic use in patients requiring MIRPE for symptomatic pectus excavatum. ■

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