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# Enhancing recovery after minimal invasive surgery of the pectus. A review of the literature

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**Abstract**: *Background***:** Pectus excavatum (PE) and pectus carinatum (PC) are the most frequent chest wall deformities presenting for a minimal invasive repair of pectus (MIRP). Enhanced recovery protocols (ERP) could improve postoperative recovery and reduce complications, however there is little uniformity in the management of patients undergoing MIRP. The aim of this review is to present an overview of the different ERPs. Our primary outcome is the effect of these ERPs on length of hospital stay (LOS), secondary outcomes include, but are not limited to, the effect on pain scores, urinary catheter requirement and duration, post-operative opioid usage and its side effects.

*Method***:** Data were collected through a Pubmed/ MEDLINE literature search. The main inclusion criterium for each study was the implementation of a clearly defined ERP consisting of a multimodal approach in a population requiring MIRP.

*Results:* In total six articles were included, each of them containing a cohort study population before and after implementing an ERP. All control groups were historical cohorts with data extracted from medical files, prior to implementation of an ERP. Thus, all articles were retrospective comparative cohort studies, with a level IV of evidence.

Most studies suggest that the implementation of an ERP could reduce LOS and reduce the incidence of urinary catheter requirement and duration, without an increase in complications. A reduction in opioid usage and the incidence of its side effects and a reduction in pain scores could not be uniformly achieved.

*Conclusion:* There is promising evidence that implementing an ERP may improve short-term outcome in a young population undergoing minimal invasive repair of pectus. Large prospective multicentred trials are needed, using proper controls and implementing multiple aspects of the ERP (pre-, peri- and postoperatively).

**Keywords**: Enhanced recovery pathway/protocol (ERP); early recovery after surgery (ERAS); pectus excavatum (PE); pectus carinatum (PC); minimal invasive repair of pectus (MIRP).

## Introduction

Pectus excavatum (PE) and pectus carinatum (PC) are the most frequent chest wall deformities presenting for surgical correction (1). PE is described as the depression of the anterior chest wall and occurs in 1 out of 400-1000 live births. PC is less common and occurs due to progressive outward growth of the anterior chest wall. Both deformities have a pronounced male predominance (2). There are two commonly known surgical techniques. The classic open "Ravitch" procedure, which involves exposure of the anterior thorax region with resection of the costal cartilages affected bilaterally combined with a transverse sternal osteotomy (3). However, after Donald Nuss published his Nuss procedure (minimal invasive repair of pectus excavatum, MIRPE) in 1998, whereby 1-3 curved bars are inserted behind the sternum to position it anteriorly, it has changed the treatment of PE and become the most commonly used technique (Fig. 5-6) (4). The severity of the pectus deformity may become more noticeable during pubertal growth spurs and repair is therefore usually performed in the teenage years. In 2005, Horatio Abramson added the Abramson procedure as a minimal invasive repair of pectus carinatum (MIRPC), in which one subcutaneously placed bar is fixed to the ribs with retrograde traction to reduce the PC.

Reasons for surgical intervention range from cardiopulmonary problems, such as chest pain,

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fatigue, dyspnoea, exercise intolerance due to compression or restriction of lung and cardiac structures and cosmetic correction (5, 6).

Even though there are smaller incisions, reduced blood loss and reduced stress response using the MIRP technique, it is still correlated with significant postoperative pain due to the constant pressure on the sternum and potential intercostal neuropraxia. Therefore, the post-operative pain management can be quite challenging (7). Notably, effective pain management in the acute post-operative period significantly influences length of hospital stay (LOS) (8). Currently there is little uniformity in the clinical management of these patients (9). Furthermore, there is little literature available on the effect of the implementation of an enhanced recovery protocol (ERP) in a paediatric population (10). Meanwhile there is also a growing tendence towards reduction of resource utilisation by reducing length of stay, without sacrificing the patient's well-being and without increasing postoperative complications. In view of these challenges, many ERPs have been proposed for MIRP. The aim of this review is to present an overview of the different ERPs. Our primary outcome is the effect of these ERPs on LOS, secondary outcomes include, but are not limited to, the effect on pain scores, urinary catheter requirement and duration, post-operative opioid usage and its side effects.

## Method

Articles for review were identified via Pubmed and Medline following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (11). Filters were used to show only articles in English, published between February 2016 and 2021, involving human patients aged between 0 and 35 years. There were no eligible studies published before 2016. The search terms "pectus", "enhanced recovery", "early recovery" and "ERAS" were used. Screening and eligibility analysis were performed by one reviewer (N.T.). Of the results yielded after the

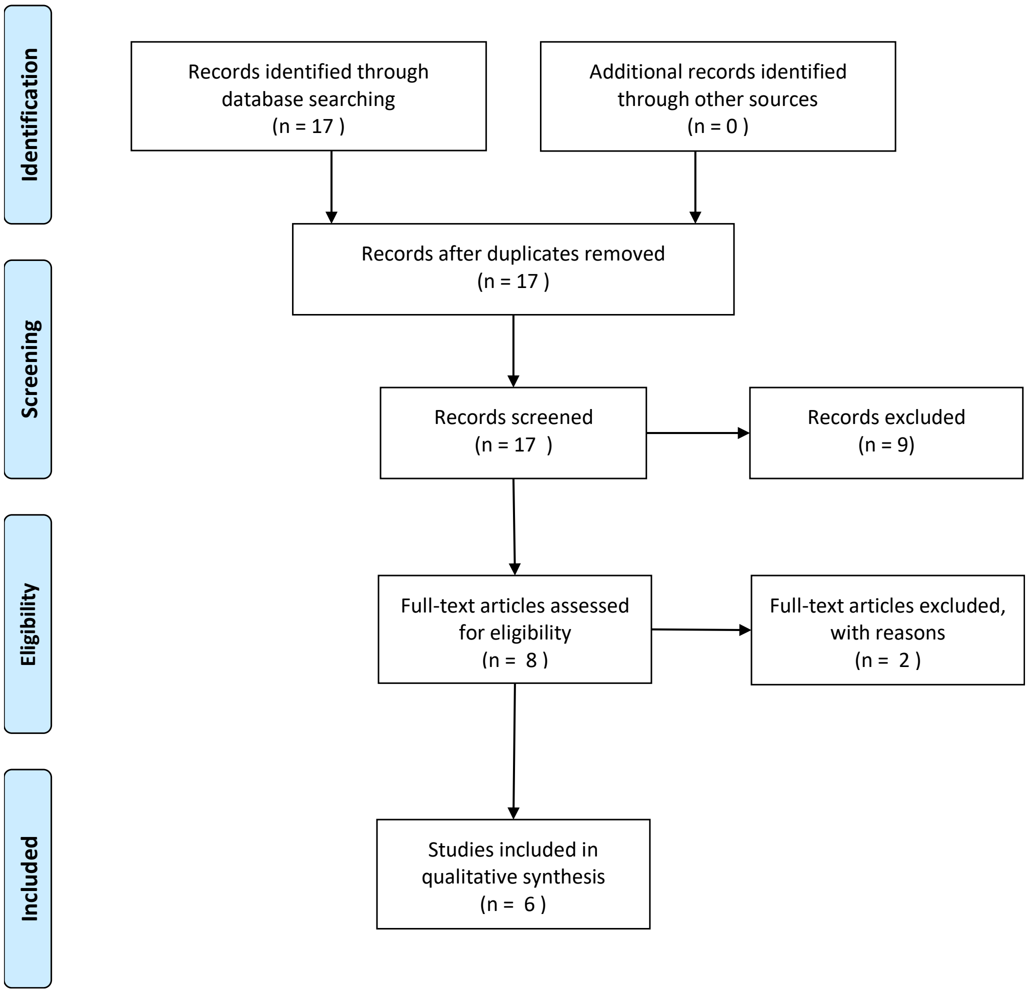


Fig. 1. — Flow chart study selection.

initial search, further screening of each title was performed using keywords such as "enhanced recovery", "perioperative management", "analgesic considerations", and "analgesia modalities". The main inclusion criterium for each study was the implementation of a clearly defined ERP consisting of a multimodal approach in a population requiring MIRP. After full-text reading, the main reasons for study exclusion included the absence of a clearly defined multimodal enhanced recovery protocol and interventions related to only singular elements of ERPs. Elements of the ERP, study population, study duration, inclusion and exclusion criteria, and primary and secondary outcomes such as LOS, pain scores, opioid requirements, and post-operative complications were reviewed in each study. The quality of conduct of each study was assessed using the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) checklist, also assessing for possible selection and information bias (12).

## Results

The initial search yielded 17 results of which 9 were excluded by screening titles and abstracts. After reading full-texts 2 more articles were excluded due to a different research scope. In total 6 articles were included, each of them containing a cohort study population before and after implementing an ERP. These articles were assessed for quality and omission using the STROBE Statement checklist for cohort studies (12). Details of this assessment can be found in Appendix 1. A flow chart of the screening process is detailed in Figure 1. An overview of the author, title, study type, population and limitations of the included studies can be found Table 1. Four studies took place in the USA (13-16), one in Belgium (17) and one in China (18). All were single centre and largely single surgeon studies.

The studies were conducted between 1998 and 2019. All control groups were historical cohorts with data extracted from medical files, prior to implementation of an ERP. Thus, all articles were retrospective comparative cohort studies, with a level IV of evidence according to Sackett et al (19). Four studies collected data from a period between 3 – 5 years (13-15, 18). Wildemeersch et al. prospectively collected data for their ERP group between June 2017 and December 2017, however they did not specify during which period they extracted data for their historical cohort (17). Holmes et al. collected data between 1998 and 2017, thus having the longest period of data collection (16). Four studies were conducted on patients who underwent MIRPE, one study by Mangat et al. also included patients undergoing the Ravitch procedure for PE, mixed PE/PC and PC (15). The study by Wildemeersch et al. included patients undergoing MIRPE as well as those who needed surgical correction of PC using Abramson's technique (MIRPC) (17). Study sizes differed between studies ranging from 41 patients to 436 patients. We limited the data extracted from the Mangat et al. study to the cohort that underwent a Nuss procedure, excluding the results of the Ravitch cohort, which is not a minimal invasive technique. This resulted in study size of 41 patients. Holmes et al. achieved a study size of 436 patient by including the patients from the transition period between the pre-ERP and the ERP periods, however we did not consider the results of the transition period in our review, reducing the study size to 332 patients. Ages were comparable between studies, with a total range between 6 and 30 years. Wharton et al. did not present exact numbers, but presented the population characteristics in charts (13). Wildemeersch et al. expressed the age range, but no mean age for their population could be found in the article (17).

The different proposed ERPs are presented in Table 2. Three studies included preoperative patient education in their ERP (13, 14, 17), of which one included aerobics and stretching exercises one month prior to surgery. Wildemeersch et al. included a preoperative web-based psychological screening and the assessment of risk for persistent postsurgical pain (PPSP). They had the longest follow-up time up to 3 months for their ERP cohort, with further assessment of risk factors using their web-based tool (17). Wildemeersch et al., Wharton et al. and Mangat et al. implemented a pre-emptive analgesic strategy using gabapentin prior to surgery. Holmes et al. introduced gabapentin into their postoperative management, they did not describe a preoperative or perioperative protocol (16). One study by Yu et al. implemented an ERP for they perioperative management, not describing a pre- or a postoperative protocol (18). All studies included acetaminophen and nonsteroidal anti-inflammatory drugs (ketorolac or ibuprofen) in their multimodal analgesic approach. Wildemeersch et al. strictly deferred the use of postoperative intravenous morphine and tramadol, instead they relied on analgesia with a patient-controlled epidural analgesia (PCEA) on top of their multimodal approach. In contrast, Litz et al. and Wharton et al. used a patient controlled narcotic analgesic (PCA) of either hydromorphone or morphine respectively, the latter also including a ketamine PCA. Mangat

*Table 1*

Overview of included articles with study type, study size, population sample, population age and limitations. ERP (enhanced recovery protocol); MIRPE (minimal invasive repair of pectus excavatum); PE (pectus excavatum); PC (pectus carinatum); PVB (paravertebral catheter).

| AUTHOR YEAR COUNTRY | JOURNAL | STUDY TYPE | STUDY SIZE | POPULATION SAMPLE | AGE, YEARS, (RANGE) | LIMITATIONS |
|---|---|---|---|---|---|---|
| **LITZ N. ET AL., 2017 USA** | Pediatric surgery international | Retro-spective compara-tive cohort study | 64 patients<br>27 pre-ERP<br>37 ERP | MIRPE between 2010-2015.<br>Pre-ERP: 2010-2012<br>ERP: 2014-2015 | Mean pre-ERP<br>15.3 ± 1.6<br>(9.9-7.6)<br>Mean ERP<br>15.5 ± 1.8<br>(8.9-18.1) | Data extracted retrospectively from medical records.<br>Unclear description of missing data, inclusion or exclusion criteria Transition period (2012-2014), possible bias towards lower opioid use Single centre |
| **WILDEMEERSCH D. ET AL. 2018 BELGIUM** | JMIR perioperative medicine | Population based cohort study | 112 patients<br>93 pre-ERP<br>29 ERP | ERP: recruitment in 2015 (June-December)<br>Exclusion criteria: psychiatric disease, chronic opioid use, revision surgery<br>Pre- ERP: Historical cohort: Age < 18 y, pathology requiring MIRP | ERP<br>- (12-18) | Retrospective data, matching only by age (<18y) and pathology (PE and PC).<br>No procedure segregated analyses (PE vs PC).<br>Single centre, single surgeon.<br>No description of opioid use. |
| **HOLMES D.M. ET AL. 2018 USA** | Journal of Pediatric Surgery | Retro-spective compara-tive study | 436 patients<br>146 pre-ERP<br>104 transition<br>186 ERP | MIRPE between January 1998 and December 2017<br>Pre-ERP 1998-2006<br>Transition 2007-2011<br>ERP 2012-2017 | Mean total<br>15 ± 2.7<br>(6.1-25.6)<br>Mean pre-ERP<br>14.2 ± 3.3<br>(-)<br>Mean ERP<br>15.3 ± 2.3<br>(-) | Retrospective design, missing data.<br>High correlation between factors ex. PVB + nursing protocol simul-taneously implemented.<br>Transition period, possible bias towards lower opioid use.<br>No rate of events for nausea/vomi-ting.<br>Single centre, largely single surgeon. |
| **MANGAT ET AL. 2020 USA** | Pediatric surgery international | Retro-spective review | 41 patients<br>13 pre-ERP<br>28 ERP | Nuss procedures between 2014 and 2018.<br>Pre-ERP (2014-2015)<br>ERP (2015-2018) | Med. pre-ERP 15 (13.5-16)<br>Med. ERP 16 (14-17) | Retrospective design (missing data and bias)<br>Single institution, small cohort |
| **WHARTON ET AL. 2020 USA** | Journal of Pediatric surgery | Retro-spective compara-tive study | 109 patients<br>51 pre-ERP<br>58 ERP | Nuss procedures between 2015 and 2018.<br>Pre-ERP (2015-2016)<br>ERP (2017-2018)<br>Exclusion: age >21 and combined surgeries. | - | Retrospective design.<br>Statistical methods not mentioned.<br>No clear presentation of popula-tion<br>Unclear how data are extracted and presented.<br>No description op opioid use.<br>No stratification based on compliance.<br>Single centre. |
| **YU ET AL. 2020 CHINA** | Journal of Thoracic Disease | Retro-spective compara-tive study | 148 patients<br>75 pre-ERP<br>73 ERP | Nuss procedures between 2016 and 2019.<br>Exclusion: patients with comor-bidities and requiring thoraco-tomy, patients with anterior chest wall severe asymmetry and depressions, chest CT showing CT index < 3.0 and mild depression patients without related symptoms, complex patients with other thoracic de-formities, patients with severe scoliosis, patients with Marfan syndrome and skin or soft tissue infection near incision, incom-plete medical record. | Total<br>15<br>(6-30) | Retrospective design<br>Small population, selection bias<br>Only comparative for perioperative protocol.<br>Single centre. |

Overview of included articles with study type, study size, population sample, population age and limitations. ERP (enhanced recovery protocol); MIRPE (minimal invasive repair of pectus excavatum); PE (pectus excavatum); PC (pectus carinatum); PVB (paravertebral catheter)

*Table 2*

Overview of enhanced recovery protocols. POD (postoperative day); LMA (laryngeal mask airway); PCA (patient controlled analgesia); PCEA (patient controlled epidural analgesia); PACU (post anaesthesia care unit); NSAID (nonsteroidal anti-inflammatory drugs).

| | LITZ ET AL. | WILDEMEERSCH ET AL. | HOLMES ET AL. | MANGAT ET AL. | WHARTON ET AL. | YU ET AL. |
|---|---|---|---|---|---|---|
| **PREOPERATIVE** | Preoperative information, education and counselling<br>Standardized analgesic protocol<br>Antimicrobial prophylaxis | Planning surgery<br>Anaesthesiology assessment.<br>Patient education<br>Activation Web-based platform<br>Start gabapentin 1 week preoperatively<br>Psychological screening<br>Risk factor assessment for increased pain | - | Carbohydrate drink 2hours prior to surgery<br>Fluid bolus<br>Multimodal pain management<br>Start gabapentin night before surgery | Patient education incl. preop handbook<br>Counselling by surgeon<br>Aerobic and back/chest stretching exercises 1 month prior to surgery<br>3 days prior to surgery<br>– Gabapentin<br>– Polyethylene glycol | - |
| **INTRAOPERATIVE** | Standardized anaesthetic protocol<br>Maintenance of normovolemia and normothermia<br>Avoidance of arterials lines, epidurals, routine ordering of blood products and perfusion services | Standardized anaesthetic protocol with epidural catheter<br>Maximal multimodal antiemetic strategy | - | Standardized anaesthetic protocol with epidural catheter | Three level bilateral intercostal nerve blocks and field block around incision<br>(intraoperative care unaltered between ERP and pre-ERP cohort) | LMA<br>Diapers instead of urinary catheter<br>Indwelling drainage of the right pleural cavity or subcutaneous with 15-F drainage |
| **POSTOPERATIVE** | Admission to medical/surgical floor<br>Standardized multimodal analgesic protocol incl. PCA<br>Nausea and vomiting prophylaxis<br>Bowel regimen<br>Urinary retention protocol<br>Early mobilization on POD 0<br>Early oral nutrition, clear liquids on POD 0<br>One postoperative chest Xray with additional imaging only as needed<br>No routine labs | "Pectusboek" with post-operative trajectory:<br>PACU until discharge criteria fulfilled<br>Standardized multimodal analgesic protocol incl. PCEA<br>Continuation gabapentin<br>Antiemetic strategy.<br>Discontinuation of PCEA on POD 6 latest.<br>ASAP removal of urinary catheter<br>Follow-up after discharge through Web based platform | Standardized multimodal analgesia incl. lidocaine infused bilateral paravertebral catheters and PCA<br>Start gabapentin<br>Early ambulation<br>Foley catheter removal<br>Diet initiation POD0 | PACU until discharge criteria fulfilled<br>Early ambulation<br>Encourage nutrition according to diet tolerance<br>Standardized multimodal pain management incl. epidural analgesia of PCA if epidural failed<br>Continuation gabapentin<br>Discontinuation epidural and urinary catheter removal POD 3 | Postsurgical handout given at discharge<br>Standardized multimodal analgesia protocol, incl. narcotic and ketamine PCA<br>Continuation gabapentin<br>Bowel regimen<br>Gut prophylaxis for chronic NSAID use | |

Overview of enhanced recovery protocols. POD (postoperative day); LMA (laryngeal mask airway); PCA (patient controlled analgesia); PCEA (patient controlled epidural analgesia); PACU (post anaesthesia care unit); NSAID (nonsteroidal anti-inflammatory drugs)

et al. implemented the use of an epidural catheter in their strategy, but also included oxycodone after discontinuation of the epidural. Holmes et al. extended their multimodal analgesic regimen with a narcotic PCA during admission and lidocaine infused bilateral paravertebral catheters that were placed perioperatively and remained until 2 to 3 days after discharge and removed at home.

Table 3 summarizes an overview of results commonly reported between studies.

LOS, our primary outcome, was significantly reduced after implementing an ERP in every study

*Table 3*

| OUTCOME | LITZ ET AL. PRE-ERP | LITZ ET AL. ERP | WILDE-MEERSCH ET AL. PRE-ERP | WILDE-MEERSCH ET AL. ERP | HOLMES ET AL. PRE-ERP | HOLMES ET AL. ERP | MANGAT ET AL. PRE-ERP | MANGAT ET AL. ERP | WHARTON ET AL. PRE-ERP | WHARTON ET AL. ERP | YU ET AL. PRE-ERP | YU ET AL. ERP |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| LOS (DAYS) | 4* | 2,8* | 6,32* | 7,66* | 4,9* | 3,1* | 5 | 5 | 3,49* | 2,897* | 7,71* | 4,96* |
| PAIN SCORE POD0 | 4,1* | 5,2* | - | - | - | - | - | - | 5,527* | 4,488* | - | - |
| PAIN SCORE POD1 | 3,2 | 3,8 | 1,24 (R) 2,84 (A) | 1,26 (R) 2,58 (A) | 4* | 3,2* | - | - | - | - | - | - |
| PAIN SCORE POD2 | 3,6 | 3,8 | 1,41 5 (R) 3,24* (A) | 1,08 (R) 2,48* (A) | - | - | - | - | - | - | - | - |
| PAIN SCORE DISCHARGE | 3,2 | 3,5 | - | - | - | - | 4 | 2 | - | - | - | - |
| OPIOID USAGE (MG $KG^{-1}$ B OR MEDD $KG^{-1}$ C) | 3,3B* | 1,2B* | - | - | 0,74C* | 0,49C* | 1,51B* | 2,61B* | - | - | - | - |
| URINAY RETENTION REQUIRING CATHETER (INCIDENCE) | 33% | 14% | - | - | 10,9% | 16,7% | 23% | 4% | 47%* | 21%* | - | - |
| URINARY CATHETER DURATION (DAYS) | - | - | 4,66* | 3,41* | 2,5* | 1,1* | 3,97* | 3,25* | - | - | - | - |
| NAUSEA (INCIDENCE) | 63% | 43% | 40%* | 17%* | - | - | 54% | 72% | - | - | - | - |
| DAYS OF NAUSEA (DAYS) | - | - | - | - | 0,7* | 1,1* | - | - | - | - | - | - |
| RETURN TO ED (INCIDENCE) | 0% | 13% | - | - | - | - | 8% | 11% | - | - | - | - |
| READMISSION (INCIDENCE) | 0% | 8% | - | - | 7,50% | 5,10% | 0% | 7% | 37,30% | 13,80% | - | - |

Overview of commonly assessed outcomes, comparing cohort without enhanced recovery protocol (pre-ERP) and with enhanced recovery protocol (ERP). Pain scores assessed according to numerical rating scales (NRS) 0= no pain, 10 worst imaginable pain. Opioid usage expressed in (B) morphine equivalents per kg (mg kg-1) or (C) morphine equivalents daily dose per kg (MEDD kg-1). (*) difference reported as significant p<0.05, (-) = no data LOS (length of stay); POD (postoperative day); R (rest); A (activity); ED (emergency department).

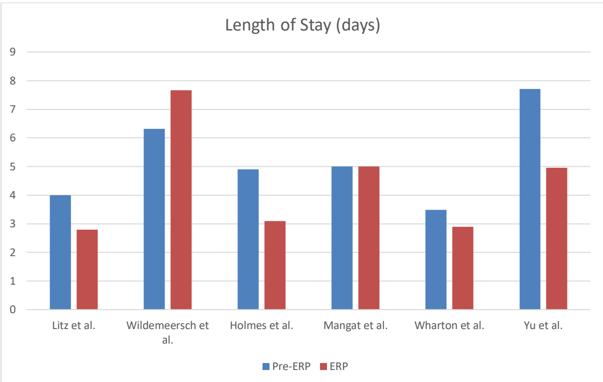


Fig. 2. — Comparing length of stay with enhanced recovery protocol (ERP) and without ERP (pre-ERP).

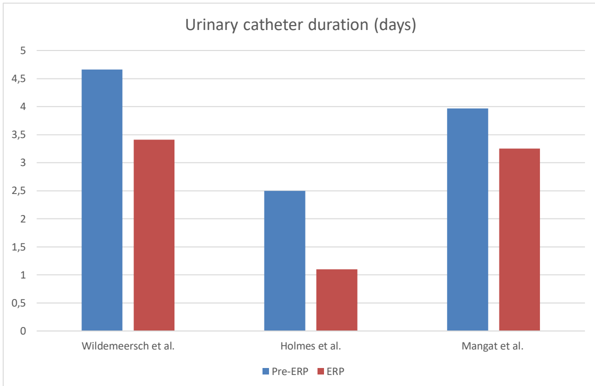


Fig. 3. — Comparing number of days requiring urinary catheter with enhanced recovery protocol (ERP) and without ERP (pre-ERP).

except two (Fig. 2) Wildemeersch et al. showed a significant increase in LOS after implementing an ERP (7.66 ± 2.01 ERP vs 6.32 ± 1.26 days pre-ERP), while Mangat et al. could produce no difference between their cohorts (17).

When looking at our secondary outcomes, pain scores were significantly higher in Litz et al.'s study in the ERP group on postoperative day (POD) 0 (4.1 ± 1.6 pre-ERP vs 5.2 ± 1.7 ERP, $p< 0.01$), only to be similar at discharge (3.2 ± 1.7 pre-ERP vs 3.5 ± 2.2 ERP, $p = 0.6$) (14). Wharton et al, however, showed a significant decrease in pain scores on POD 0 (5.527 pre-ERP vs 4.488 ERP, $p = 0.0065$). Other postoperative days failed to show a difference after implementation of their ERP (13). There was a significant reduction in pain scores after protocol implementation at all time points except the morning of POD 3 in the study by Holmes et al., but no significant difference could be found at discharge. They did not present exact scores, except for the morning after surgery (4.0 ± 2.0 pre-ERP vs 3.2 ± 1.4 ERP) (16).

Opioid usage was quantified in three studies. Litz et al. and Mangat et al. calculated morphine equivalents (ME, mg $kg^{-1}$), while Holmes et. al used morphine equivalent daily dose per kg (MEDD $kg^{-1}$). Litz et al. and Holmes et al. showed a reduction in opioid usage (3.3 ± 1.4 mg $kg^{-1}$ pre-ERP vs 1.2 ± 0.5 mg $kg^{-1}$ ERP, $p < 0.01$; 0.74 ± 0.77 MEDD $kg^{-1}$ pre-ERP vs 0.49 ± 0.20 MEDD $kg^{-1}$ ERP, $p < 0.05$ respectively), while Mangat et al. reported a significant increase of opioid usage (1.51 mg $kg^{-1}$ pre-ERP vs 2.61 mg $kg^{-1}$ ERP, $p = 0.02$).

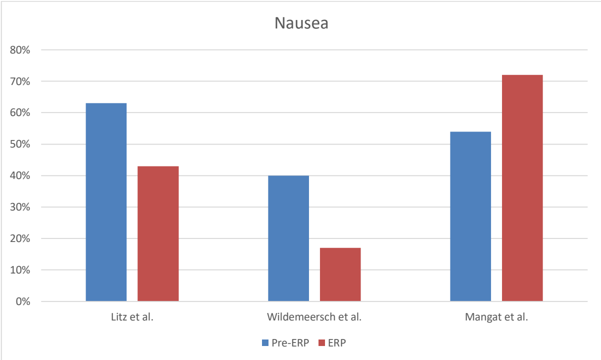


Fig. 4. — Comparing incidence of nausea with enhanced recovery protocol (ERP) and without ERP (pre-ERP).

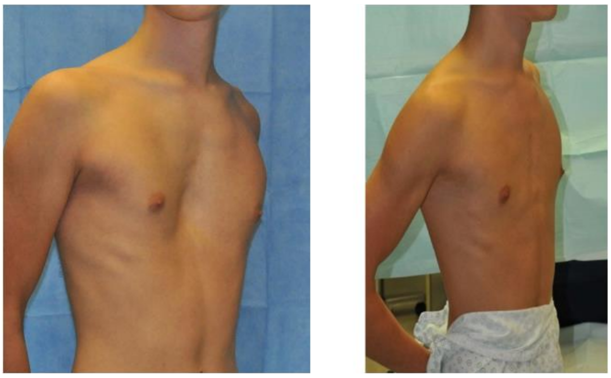

Fig. 5. — Patient with pectus excavatum before (left) and after (right) Nuss procedure.

Fig. 6. — Chest X-ray showing anterior and lateral view after correction of pectus excavatum using Nuss procedure.

Urinary retention requiring catheterization was mentioned in four studies. Litz et al. reported a decrease in incidence, but this decrease was not significant (33% pre-ERP vs 14% ERP, p= 0.07). Similar results were produced by Wharton et al. with a significant reduction in incidence (41% per-ERP vs 21% ERP, p= 0.0044). Mangat et al. also showed reduction in need for urinary catheterization, while Holmes et al. reported an increased need. Both results were of insignificant value (Fig. 3) Three studies discussed the duration of indwelling urinary catheter (IDUC), all of which showed a significant reduction in duration (15-17). Notably, Yu et al. refrained from placing an IDUC and used diapers perioperatively instead (18).

When considering nausea postoperatively, two studies showed a decrease in incidence after ERP implementation, with a significant reduction from 40% to 17% (p= 0.3) in the study of Wildemeersch et al.(17). However, in Mangat et al.'s study the incidence was higher after ERP implementation, although this was not significant (15). Unlike Wildemeersch et al. they did not include an anti-emetic strategy in their ERP . Holmes et al. did not report incidence of nausea, but days of nausea. In their study, there was an increase of days of nausea after ERP implementation (0.7 ± 1.2 pre-ERP vs 1.1 ± 1.2 ERP, p <0.05) (16) (Fig. 4)

With reducing LOS one must also take into account that patients may return to the emergency department or need readmission, due to "late" complications or uncontrollable pain. Holmes et al. and Wharton et al. showed a reduction in re-admissions (7.5% vs 5.1% p = 0.2; 37.3% vs 13.8% respectively) (13, 16). In contrast, Litz et al. and Mangat et al. reported no readmissions in their pre-ERP cohort compared to 8% and 7% in their ERP cohort respectively.

## Discussion

With enhanced recovery protocols gaining popularity in different types of surgery, it may be interesting to focus on the applicability of this on MIRP and on its relatively young population. Promising evidence is emerging showing that a paediatric population could also benefit from an ERP in different types of surgery (10). Furthermore, there is a growing tendence towards reduction of resource utilisation by reducing length of stay, without sacrificing the patient's well-being and without increasing postoperative complications. After the results of the study conducted by Wildemeersch et al. in our centre, we implemented an ERP with preoperative, perioperative and post-operative elements increasing adherence in the different departments. However, due to the reduced availability of monitoring tools and lack of psychosocial resources, the web-based monitoring application has been left out of the ERP, which is still standard of care (17).

All but two studies presented a significant reduction in LOS, of which two also showed a decrease in opioid usage, thus possibly also a reduction in resource utilisation. However, Litz et al. and Holmes et al. both implemented a transition period between the pre-ERP and the ERP cohort, allowing them time to alter their ERP towards a lower narcotics usage and a lower LOS. This transition period may potentially bias study results toward the desired outcomes (14, 16). Yu et al. implemented strict exclusion criteria for their study population as summarized in Table 1, creating the opportunity for a selection bias with the preferred outcome of reducing LOS (18). Wildemeersch et al. showed an increase in LOS, they however mentioned most patients could have been discharged earlier (6.59 days p=0.40), but stayed in the hospital for nonmedical reasons (17). This further underlines the need for biopsychosocial management strategies, such as discussing patient expectations preoperatively.

While the study conducted by Wharton et al. showed promising results with a reduction in LOS, pain scores, urinary retention requiring catheterization and less readmissions, it remains unclear which statistical analyses they used on their data. Precise measurement op opioid usage was not conducted in their analysis, although they mention to explore it in a further examination of their data (13). Mangat et al. (15) could not produce the desired outcome with their ERP. They contributed the lower pain scores at discharge to the increased opioid usage in their ERP cohort.

Every proposed protocol is unique in its combination of interventions, although some interventions are found in most, if not all of the protocols, such as the use of acetaminophen and NSAIDs. It could be interesting to compare the different analgesic strategies implemented in these studies. There is a *lack of evidence* showing which analgesic modality is superior for MIRP. In a study by Schlatter et al. (20) comparing three analgesia modalities (epidural vs PCA and intercostal nerve block vs scheduled oral pain meds and intercostal nerve blocks), they were able to reduce LOS from 4.4 days with epidural analgesia to 1.6 days with oral pain medication and an intercostal nerve block. They also mention that an enhanced preoperative consultation, patient education and setting the right expectations might be as important as the analgesic modality used for the reduction in LOS and pain scores. This philosophy was also applied by Wildemeersch et al. and Holmes et al. (16, 17), with the first also screening for preoperative risk factors. When comparing epidural analgesia to PCA, a meta-analysis from 2014 including 3 randomized controlled trials (RCT) and 3 retrospective cohorts concluded that epidural analgesia may initially provide superior pain control, however without any significant difference secondary outcomes such as LOS, adverse event, opioid side-effects and epidural complications (21). Currently, there a few centres implementing intercostal cryoanalgesia for analgesia after MIRP. A small single institution randomized clinical trial (22) compared intercostal cryoanalgesia to epidural analgesia after a Nuss procedure. Their data showed that cryoanalgesia resulted in reduction in LOS and systemic opioid consumption, while providing equivalent pain control. Comparable results were found in a study by Harbaugh et al. (23), where there was a reduction in LOS and an increased perioperative opioid use in the cryoanalgesia cohort, but no difference in postoperative narcotic requirements. Furthermore, there was a reduction in prescription doses of opioids after intercostal cryoablation vs epidural. However, patients can develop neuralgias and numbness up to 2 months after surgery with a gradual return of sensation presumably during axonal regeneration of the intercostal nerve (20). More RCTs are required to assess if this analgesic approach could be implemented in future ERPs. Currently, there is a clinical trial in the Children's Hospital Colorado which started in May 2020, aiming to compare the use of video-assisted intercostal nerve cryoablation, erector spinae block, and thoracic epidural for postoperative analgesia after MIRPE (https://clinicaltrials.gov/ct2/show/NCT04211935).

The risk of developing PPSP is quite high after pectus surgery, as described by Williams et al., where higher pain scores during the first 3 post-operative days and at 2 weeks predicted slower recovery and higher pain scores at 4 and 12 months (24). Therefore it might be interesting to asses if the proposed ERPs could also affect the incidence of PPSP although there is limited data on the precise incidence in children after MIRP. Furthermore, pragmatic studies that asses the feasibility of implementation of an ERP and include long-term patient related outcome measurements could be of value, such as the one conducted in our centre by Wildemeersch et al.

Limitations of our review is that we only included six studies, of which one was conducted in our own centre. We also focused exclusively on MIRP technique, the most commonly conducted technique in our centre, which rendered a smaller study population. The studies presented are all limited by their small study population and their retrospective design, with a historical control cohort, creating opportunity for selection bias.

The question could also arise if the proposed ERPs are universally applicable, seeing all of them are implemented in a single centre, with the surgery largely done by one specific surgeon. Because all ERPs contains both similar and very different analgesic modalities, it is difficult to extract which specific elements of the ERP is superior. We must also address the likelihood of publication bias of reports demonstrating no efficacy of ERPs in MIRP.

It would be inappropriate to propose a proper universal protocol with such limited evidence. Thus, it is cautious to conclude that the implementation of an ERP could significantly reduce resource utilisation such as LOS and opioid usage and improve outcome.

## Conclusion

There is promising evidence that implementing an enhanced recovery protocol may improve short-term outcome in a young population undergoing minimal invasive repair of pectus. Large prospective multicentred trials are needed, using proper controls and implementing multiple aspects of the ERP (pre-, peri and postoperatively). Furthermore, more research is needed to assess which analgesic modality is superior and should be implemented in an ERP.

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**Appendix 1. Assessment of articles according to 22 point STROBE checklist items**

| ITEM NO | LITZ ET AL. | WILDEMEERSCH ET AL. | HOLMES ET AL. | MANGAT ET AL. | WHARTON ET AL. | YU ET AL. |
|---|---|---|---|---|---|---|
| **1A** | 1 | 1 | 1 | 1 | 1 | 1 |
| **1B** | 1 | 1 | 1 | 1 | 1 | 1 |
| **2** | 1 | 1 | 1 | 1 | 1 | 1 |
| **3** | 1 | 0 | 1 | 1 | 1 | 1 |
| **4** | 1 | 1 | 1 | 1 | 1 | 1 |
| **5** | 1 | 1 | 1 | 1 | 1 | 1 |
| **6A** | 0 | 1 | 1 | 1 | 1 | 1 |
| **6B** | 1 | 1 | 0 | 0 | 0 | 0 |
| **7** | 0 | 0 | 1 | 1 | 1 | 1 |
| **8** | 0 | 1 | 1 | 1 | 0 | 1 |
| **9** | 0 | 1 | 0 | 0 | 0 | 1 |
| **10** | 1 | 1 | 1 | 1 | 1 | 1 |
| **11** | 0 | 1 | 1 | 1 | 0 | 1 |
| **12A** | 1 | 1 | 1 | 0 | 0 | 1 |
| **12B** | 0 | 0 | 0 | 1 | 0 | 1 |
| **12C** | 0 | 0 | 0 | 0 | 0 | 1 |
| **12D** | 0 | 0 | 0 | 0 | 0 | 1 |
| **12E** | 0 | 0 | 0 | 0 | 0 | 0 |
| **13A** | 1 | 1 | 1 | 1 | 1 | 1 |
| **13B** | 0 | 1 | 0 | 0 | 0 | 1 |
| **13C** | 0 | 0 | 0 | 0 | 0 | 1 |
| **14A** | 1 | 0 | 1 | 1 | 1 | 1 |
| **14B** | 0 | 1 | 1 | 0 | 0 | 0 |
| **14C** | 1 | 1 | 0 | 1 | 1 | 0 |
| **15** | 1 | 1 | 1 | 1 | 1 | 1 |
| **16A** | 1 | 1 | 1 | 1 | 0 | 1 |
| **16B** | 0 | 1 | 0 | 0 | 0 | 1 |
| **16C** | 0 | 1 | 1 | 0 | 0 | 0 |
| **17** | 0 | 0 | 1 | 1 | 0 | 0 |
| **18** | 1 | 1 | 1 | 1 | 1 | 1 |
| **19** | 1 | 1 | 1 | 1 | 1 | 1 |
| **20** | 1 | 1 | 1 | 1 | 1 | 1 |
| **21** | 1 | 1 | 1 | 1 | 1 | 1 |
| **22** | 1 | 1 | 0 | 1 | 0 | 1 |

0 = incomplete, 1 = complete. Explanation of each item can be found further in this appendix.