Postoperative consumption of opioid analgesics following correction of pectus excavatum is influenced by pectus severity: a single-centre study of 236 patients undergoing minimally invasive correction of pectus excavatum

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Abstract

Objective: Surgical correction of pectus excavatum (PE) is primarily performed to achieve cosmetic and psychological benefits for the patient. Minimally invasive repair of PE is often associated with severe postoperative pain. This study estimates the effect of the severity of PE on the postoperative consumption of opioid analgesics following this procedure to optimise pain management. Methods: A retrospective study was conducted on 236 consecutive patients undergoing minimally invasive repair of PE from 2005 to 2008. The collected data included depth of preoperative pectus excavation, patient demographics, peri- and postoperative information, including data on pain management. The consumption of opioid analgesics was registered after discontinuation of epidural analgesia and other types of opioid analgesics used during the study period were converted to morphine equivalents. Multiple linear regression analysis was performed to estimate the effect of the severity of PE on the postoperative consumption of opioid analgesics and to adjust for potential confounding. Results: The total morphine consumption following minimally invasive repair of PE ranged between 20 and 370 mg day⁻¹. Multiple linear regression analysis explained approximately 30% of the variation in daily morphine consumption (R-squared = 0.2957). There was a significant positive linear relationship between pectus severity and the daily consumption of morphine. Thus, postoperative consumption of morphine increased by 6% (95% confidence interval (CI): 0.3—11%) when preoperative PE depth deteriorated with 1 cm. Conclusion: This study confirms that pectus severity has a significant impact on the consumption of opioid analgesics following minimally invasive repair of PE. We conclude that knowledge of pectus severity might be useful in the prediction of the expected morphine consumption in future patients, especially during the critical transition period from epidural analgesia to oral analgesia.

1. Introduction

Pectus excavatum (PE) occurs in approximately 1 out of 400 live births, making it the most common congenital chest-wall deformity. PE is primarily treated to achieve anatomical correction and thus avoid cosmetic and psychological inconveniences for the patient [1]. In recent years, correction of PE has been performed using a minimally invasive surgical technique developed by Dr Nuss in the 1990s [2]. The technique has been regularly modified but it basically consists of inserting one or more convex steel bars under the sternum through small bilateral incisions in the thoracic wall [3]. Although minimally invasive surgery has been proven to reduce the surgical stress response after various types of surgery [4], minimally invasive correction of pectus excavatum (MIRPE) remains associated with severe postoperative pain [5]. The degree of postoperative pain following MIRPE has been shown to be the overriding factor in the patient’s perception of the quality of the postoperative course [6,7]. Children and adolescents have even accepted a greater degree of postoperative nausea and vomiting for the benefit of improved pain management following MIRPE [8]. In addition, pain management following MIRPE have been shown to affect all measurable objective outcomes during hospitalisation, including the capacity for deep breathing, the ability to move, the ability to eat and the length of hospital stay [6,7].
In general, insufficient pain control commonly persists after surgery [9]. Sufficient pain control not only reduces discomfort, distress and anxiety in the early postoperative period, but it is also crucial to reduce morbidity, mortality, length of hospital stay, economic costs and risk of developing chronic pain conditions [10].

The purpose of this study was to quantify the effect of preoperative assessment of pectus severity on postoperative consumption of opioid analgesics following MIRPE to optimise postoperative pain management for future candidates for PE surgery.

2. Materials and methods

2.1. Study design

This retrospective study was conducted on 236 consecutive patients undergoing MIRPE on a cosmetic indication from May 2005 through July 2008. The study was based on information from medical records and postoperative registrations from hospital-based patient data management systems.

2.2. Study population/inclusion criteria

A total of 236 consecutive patients underwent MIRPE on a cosmetic indication from May 2005 through July 2008.

2.3. Exclusion criteria

1. Patients who previously underwent surgical correction of PE (n = 2).
2. Patients who preoperatively did not receive an epidural catheter (n = 1).
3. Patients who were re-operated upon during the study period (n = 5).
4. Patients who preoperatively used opioid analgesics on a daily basis (n = 1).

2.4. Data collection

Collected data included evaluation of preoperative pectus excavation depth, pectus symmetry as well as pain related to PE, patient demographics, data on the perioperative period in terms of duration of both anaesthesia and surgery and number of inserted pectus bars as well as data for the early postoperative period, including postoperative complications and postoperative pain management. The severity of PE was evaluated by objective measurement of the distance between the deepest point of the pectus excavation and expected location of the patient’s sternum after the insertion of a convex steel bar. All preoperative evaluations were performed by the same surgeon (HKP). Consumption of opioid analgesics was registered during a 24-h period, 6 h after discontinuation of thoracic epidural analgesia. The different types of opioid analgesics used during the study period were converted to morphine equivalents.

2.5. Anaesthesia and epidural analgesia

Using local anaesthesia and a paramedian approach, an epidural catheter was placed using a hanging drop technique. The epidural catheter was most frequently placed at the thoracic (Th) level 4–6. The epidural block were activated and tested with injection of 0.5% ropivacaine or bupivacaine with simultaneous intravenous infusion of a 6% hydroxyethyl starch. General anaesthesia was initiated with intravenous injection of fentanyl (0.05–0.1 mg), propofol (1.5–2.5 mg kg\(^{-1}\)) and cisatracurium (0.1–0.15 mg kg\(^{-1}\)).

Following surgery, the thoracic epidural block was maintained with continuous epidural infusion of either 0.125–0.33% ropivacaine ± sufentanil (1 μg ml\(^{-1}\)) or 0.17–0.25% bupivacaine ± morphine (50 μg ml\(^{-1}\)). Maximum infusion rates for both types of infusions were 10 ml h\(^{-1}\). Supplementary oral pain management was initiated with acetaminophen and ibuprofen at the day of surgery.

2.6. Surgical procedure

The surgical technique has previously been described in detail [11]. The steel bars inserted were generally 5–8 cm shorter than those recommended by Nuss et al. [2] A stabiliser was normally placed on the left side of the bar as close as possible to the bar’s entry point into the chest to avoid rotation. In addition, the bar was secured on the right side by two or three 0-polydioxanone sutures (PDS, Ethicon, Somerville, NJ, USA) around the ribs. An additional bar was introduced if the desired cosmetic result was not obtained with a single bar. If the patient presented with an asymmetric PE, the bar was bent asymmetrically according to the method described by Park et al. [12]. All surgical procedures in this study were performed by the same surgeon (HKP).

2.7. Statistical analyses

Continuous normally distributed data are presented as means ± standard deviation (SD), while continuous non-normally distributed data are presented with median and inter quartile range (IQR). Multiple linear regression analysis was used to:

1. Predict postoperative consumption of opioid analgesics for a known pectus severity.
2. Assess the effect of pectus severity on postoperative consumption of opioid analgesics adjusted for potential confounders.

Independent variables included in the multiple linear regression analysis were chosen a priori based on the current knowledge about risk factors for post-surgical pain and clinical experience. The requirements for linear regression were fulfilled. \(P\)-values <0.05 were considered as statistically significant. Data were analysed using Stata/IC 10.1 for Windows (StataCorp LP, College Station, TX, USA).

3. Results

The study population consisted of 236 patients between 7 and 47 years of age, with a median age of 17.0 years (IQR, 15.1–21.7 years) (Table 1). The male:female ratio was approximately 6:1. Patients weighed from 25 to 106 kg with an average weight of 65.6 ± 13.5 kg. Just over one-quarter of
the patients had an asymptomatic pectus and around one-fifth of the patients complained preoperatively about pain or discomfort related to PE. The PE depth ranged from 2 to 10 cm with a median depth of 5 cm (IQR, 4—5 cm).

All surgical procedures were performed on a cosmetic indication, and the majority of patients (73%) achieved a satisfactory correction of PE with the insertion of one bar (Table 2). The duration of surgery ranged between 16 and 108 min with a median duration of 33 min (IQR, 28—45 min). Median duration of anaesthesia was 112 min (IQR, 99—125 min). Length of hospital stay ranged between 3 and 10 days with a median length of 5 days (IQR, 4—5 days).

The most common anaesthesiological complication in the early postoperative period was dysfunction of the epidural catheter, resulting in catheter replacement in 37 patients (16%). This percentage represented both unintended discontinuation of epidural analgesia as well as technical problems with obtaining a satisfactory epidural block because of either a unilateral block or a lack of segmental coverage. The most common surgical complication in the early postoperative period was pneumothorax (52%); this required insertion of a chest tube in five patients (2.1%). Wound infections were observed in three patients (1.3%), hydrothorax requiring drainage using a pigtail catheter in two patients (0.8%) and pneumonia demanding antibiotic treatment in one patient (0.4%).

A quarter to one-third of the patients who initially received an epidural infusion of either ropivacaine—sufentanil or bupivacaine—morphine were switched to pure ropivacaine or pure bupivacaine due to side effects, most commonly nausea and vomiting and pruritus. Median duration of epidural infusion was 93 h (IQR, 74—98 h) (Table 3).

The most commonly used opioid analgesic in the early postoperative period was oxycodone (43%) followed by fentanyl (30%). The other types of opioid analgesics used in the study period were tramadol (25%), niconmorphine and morphine (Table 4). Several patients (64%) had the need for additional analgesics. The most frequently used opioid analgesic for this purpose was oxycodone (60%), followed by tramadol (27%). Daily morphine consumption ranged between 20 and 370 mg with a median consumption of 115 mg day$^{-1}$ (IQR, 70—140 mg day$^{-1}$). Approximately one-sixth of the total consumption of morphine was administered as-needed.

Table 5 presents the results of a multiple regression analysis where predictive factors are included alongside pectus severity. Approximately 30% of the variability of the consumption of morphine was accounted for by the variables in the model (coefficient of determination equals 0.2954). Postoperative consumption of morphine was increased by 6% (95% confidence interval (CI): 0.3—11%) when preoperative PE depth deteriorated with 1 cm. Compared with morphine consumption in patients aged 12—18 years was increased by 75% and for patients over 18 years of age by 119%. Compared with

### Table 1
Preoperative patient demographics ($n=236$).

| Characteristics                  | Patients | Missing* |
|----------------------------------|----------|----------|
| Gender, no. (%)                  |          |          |
| Males                            | 203 (86) |          |
| Females                          | 33 (14)  |          |
| Age, median (IQR), years         | 17.0 (15.1—21.7) |          |
| Height, median (IQR), cm         | 180 (174—186) | 19 (8)   |
| Weight, mean ± SD, kg            | 65.6 ± 13.5 | 11 (5)   |
| Pectus severity, median (IQR), cm| 5 (4—5)  | 8 (3)    |
| Pectus symmetry, no. (%)         |          |          |
| Symmetric                        | 165 (72) |          |
| Asymmetric                       | 65 (28)  |          |
| Pain related to pectus excavatum, no. (%) | 46 (20) |          |

* Observations with missing data, no. (%); IQR: inter quartile range; SD: standard deviation.

### Table 2
Peri- and postoperative data ($n=236$).

| Characteristics | Patients | Missing* |
|-----------------|----------|----------|
| Perioperative variables, median (IQR) |          |          |
| Duration of anesthesia, min | 112 (99—125) | 71 (30) |
| Duration of surgery, min | 33 (28—45) | 20 (8) |
| Number of inserted pectus bars (%) |          |          |
| 1                | 172 (73) |          |
| 2                | 64 (27)  |          |
| Early postoperative complications |          |          |
| Pneumothorax, no. (%) | 5 (2.1) |          |
| Wound infection, no. (%) | 3 (1.3) |          |
| Pneumonia, no. (%) | 1 (0.4) |          |
| Hydrothorax, no. (%) | 2 (0.8) |          |
| Dysfunction of epidural catheter, no. (%) | 37 (16) |          |
| Length of hospital stay, median (IQR), days | 5 (4—5) |          |

* Observations with missing data, no. (%).

* Complications requiring anaesthesiological, surgical or medical intervention; IQR: inter quartile range; SD: standard deviation.

### Table 3
Postoperative epidural analgesia and consumption of non-opioid analgesics ($n=236$).

| Characteristics | Patients | Missing* |
|-----------------|----------|----------|
| Preoperative placement level of the epidural catheter, no. (%) |          |          |
| Th 3—4          | 13 (7)   |          |
| Th 4—5          | 60 (32)  |          |
| Th 5—6          | 80 (43)  |          |
| Th 6—7          | 31 (17)  |          |
| Th 7—8          | 2 (1)    |          |
| Type of epidural infusion, no. (%) |          |          |
| 0.125—0.33% ropivacaine + 1 µg sufentanil/ml | 66 (28) |          |
| 0.125—0.33% ropivacaine | 116 (50) |          |
| 0.25% bupivacaine + 50 µg morphine/ml | 38 (16) |          |
| 0.25% bupivacaine | 13 (6) |          |
| Epidural infusion rate, mean ± SD, ml/h | 6.8 ± 1.5 | 4 (2) |
| Duration of epidural infusion, median (IQR), h | 93 (74—98) | 72 (31) |

* Observations with missing data, no. (%); IQR: inter quartile range; SD: standard deviation.
patients aged 12–18 years, morphine consumption in patients over 18 years of age was increased by 25%. An increase in weight of 1 kg increased morphine consumption by 0.9% (95% CI: 0.3—1.5%). After adjusting for pectus severity, age, weight and gender, the recipients of epidural infusions containing opioid analgesics had an increase in morphine consumption equivalent to 16% (95% CI: 2—31%) compared with those who only received an infusion of local anaesthetics; IQR: inter quartile range.

The study also found a correlation between age and morphine consumption; thus, morphine consumption compared with patients aged 7—11 years was significantly increased for patients aged 12—18 years (75%) and for patients over 18 years of age (119%). Compared with patients aged 12—18 years, morphine consumption in patients over 18 years of age was increased by 25%. Not unexpectedly, there was also a significant linear relationship between weight and consumption of opioid analgesics; thus, morphine consumption was increased by 0.9 kg\(^{-1}\) (95% CI: 0.3—1.5%). Finally, morphine consumption depended on the type of previous epidural pain management. Patients who had consistently received epidural infusions of either ropivacaine—sufentanil or bupivacaine—morphine consumed 16% more morphine than patients who had primarily received epidural infusion of either ropivacaine or bupivacaine alone. The study found a trend towards increased consumption of opioid analgesics of approximately 6% among women compared with men. Morphine consumption could be estimated within the range of \(\pm 10\) mg day\(^{-1}\) for the average patient.

The daily consumption of morphine varied between 20 and 370 mg day\(^{-1}\) despite the immediate homogeneity of the patient category. The large spread in the consumption of morphine reflects the well-known inter- and intra-individual differences among patients’ response to different opioid analgesics. Several factors contribute to these differences including route of administration, half-life of the drugs used, bioavailability and drug interaction [13].

Knowing that the length of the inserted bars used at our institution was generally 5—8 cm shorter than those recommended by Huss et al. [2], study population, surgical procedure, complication rate and length of stay did not differ significantly compared with previous studies. Duration of surgery in our study, however, proved to be shorter [5]. The low complication rate in our study was consistent with what was previously reported [3,5] and was presumably attributable to the fact that our study period did not include the early learning curve, and all surgical procedures were, moreover, performed by the same surgeon (HKP).

There are a number of objective imaging methods for assessing severity of PE, including the Haller index. The Haller index relies on the ratio of the transverse and the

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**Table 4**

Postoperative consumption of opioid analgesics (n = 236).

| Characteristics                  | Patients     |
|----------------------------------|--------------|
| Management of opioid analgesics, type, no. (%) |              |
| TD fentanyl                      | 69 (30)      |
| PO oxycodeone                    | 101 (43)     |
| PO nicomorphine                  | 3 (1)        |
| PO morphine                      | 3 (1)        |
| PO tramadol                      | 60 (25)      |
| Daily dosage of morphine\(^a\), median (IQR), mg/day | 80 (60—120) |
| As-needed administration of opioid analgesics, type, no. (%) |              |
| TM fentanyl                      | 7 (5)        |
| PO oxycodeone                    | 90 (60)      |
| PO nicomorphine                  | 9 (6)        |
| PO morphine                      | 3 (2)        |
| PO tramadol                      | 41 (27)      |
| Daily as-needed dosage of morphine\(^a\), median (IQR), mg/day | 20 (10—40)  |
| Total daily dosage of morphine\(^a\), median (IQR), mg/day | 115 (70—140) |

\(^a\) Daily consumption of opioid analgesics converted to morphine equivalents; TD: transdermally administered; PO: orally administered; TM: transmurally administered; IQR: inter quartile range.

**Table 5**

Multiple linear regression analysis. Dependent variable: Log(morphine, mg/day).

| Characteristic                      | Coefficient | SE\(^a\) | P > t   | 95% CI\(^b\) |
|------------------------------------|-------------|----------|---------|--------------|
| Severity of pectus excavatum (cm)  | 0.0553      | 0.0263   | 0.037   | 0.0035 to 0.1071 |
| Age-group (12—18 years)            | 0.5572      | 0.1956   | 0.005   | 0.1716 to 0.9427 |
| Age-group (+18 years)              | 0.7829      | 0.2108   | 0.000   | 0.3674 to 1.1984 |
| Weight (kg)                        | 0.009       | 0.003    | 0.003   | 0.0031 to 0.0149 |
| Gender (female)                    | 0.0580      | 0.1018   | 0.369   | —0.1427 to 0.2588 |
| Type of epidural analgesia (+opioid analgesics) | 0.1442 | 0.0652   | 0.028   | 0.0156 to 0.2727 |
| Intercept                          | 3.002       | 0.2594   | 0.000   | 2.4906 to 3.5134 |

\(^a\) Standard error.

\(^b\) 95% confidence interval.
The use of non-opioid analgesics has previously been described both in combination with epidural pain management and as part of the long-term pain treatment following MIRPE [3,5]. Regarding the use of opioid analgesics following MIRPE, morphine has previously been described in the management of breakthrough pain during hospitalisation. Oxycodone has been used in the treatment of postoperative pain at and following discharge [3]. To our knowledge, no studies have described the use of fentanyl in late postoperative pain management following MIRPE. We have not been able to find published studies concerning the consumption of opioid analgesics following MIRPE either generally or specifically in the critical transition period between epidural and oral analgesia following MIRPE. Thus, it remains unclear whether the consumption of non-opioid analgesics and opioid analgesics in our study is smaller than, equal to or greater than the consumption at other facilities offering minimally invasive correction of PE.

In a small study of 14 patients following MIRPE, Coln et al. [6] found that the two patients with the highest pain scores during and after hospital discharge needed long-term postoperative pain management (2 months and 4 months, respectively), and they both had severe pectus excavations (Haller index 5.2 and 8.5, respectively). The significant positive linear relationship between preoperatively assessed pectus severity and consumption of opioid analgesics following MIRPE in our study was similar to the positive correlation between the severity of PE and the necessary force to elevate the sternum identified by Fonkalsrud and Reemtsen in a prospective study of 44 consecutive patients aged 4–53 years undergoing a modified Ravitch correction of PE [18].

The differences in morphine consumption for different age groups identified in our study may partly be explained by age-related rigidity in the thoracic cage supported by the findings of Weber et al. [19] and Nagasao et al. [20]. Weber et al. [19] found in a study of 100 consecutive patients with symmetric PE that the traction needed for elevation of the sternum depended on patient age, while Nagasao et al. [20] found that the intensity and distribution of the stress on the thorax following MIRPE depended on patient age. Furthermore, in a retrospective study of the surgical outcome following MIRPE by Kim et al. [21], the proportion of patients who complained of chest pain 6 months after MIRPE was greater in adult patients aged 20–52 years (55%) compared with children aged 18 months to 12 years (4%). By contrast, Molik et al. [22] found that age did not affect the need for analgesics following MIRPE in a comparative study of MIRPE versus open surgery for correction of PE. The results of the

| Table 6 Estimation of expected postoperative consumption of morphine after discontinuation of thoracic epidural analgesia with a combination of local analgesics and opioid analgesics (male gender). |

| Severity of pectus excavatum (cm) | Consumption of morphine (mg/day) (95% confidence interval) |
|-----------------------------------|-----------------------------------------------------------|
| Age-group 7–11 years (35 kg)      | Age-group 12–18 years (62 kg)                             | Age-group +18 years (74 kg) |
| 2                                 | 36 (24–54)                                                | 79 (66–94)                  | 110 (91–133) |
| 3                                 | 38 (25–56)                                                | 84 (73–96)                  | 117 (101–136) |
| 4                                 | 40 (27–59)                                                | 88 (80–98)                  | 123 (110–139) |
| 5                                 | 42 (28–63)                                                | 93 (85–102)                 | 130 (117–145) |
| 6                                 | 44 (30–67)                                                | 99 (89–110)                 | 138 (122–155) |
| 7                                 | 47 (31–72)                                                | 104 (91–120)                | 146 (126–169) |
| 8                                 | 50 (32–77)                                                | 110 (92–133)                | 154 (128–186) |
| 9                                 | 52 (33–84)                                                | 117 (92–147)                | 163 (129–205) |
| 10                                | 55 (34–91)                                                | 123 (93–163)                | 172 (130–227) |
latter are not directly comparable with the results of our study because the 35 patients included had an average age of just 9.5 years (range 5–20 years).

Our study found a positive linear relationship between weight and need for morphine, which seems both biologically plausible and consistent with clinical practice where dosing of analgesics is usually based on a combination of a standard dosage and an individual dosage depending on drug effect. Early postoperative pain management consisting of thoracic epidural block proved to have an impact on the subsequent use of orally and transdermally administered opioid analgesics. We suggest that the reason for this difference could be found in problems concerning the development of opioid tolerance. Thus, continuous epidural infusion of either morphine or sufentanil is likely to have influenced the subsequent consumption of systemic opioid analgesics. Opioid tolerance has been shown to develop rapidly in animal studies, but it is unclear whether significant tolerance to opioid analgesics occurs following human clinical treatment of both acute and chronic pain [23]. There is clinical evidence that opioid tolerance rapidly occurs when using opioid-based anaesthesia; this can result in postoperative hyperalgesia and increased consumption of opioid analgesics [24]. Other studies indicate that opioid tolerance does not develop in the perioperative period [25]. To our knowledge, no studies have examined either the speed of the potential development of opioid tolerance or the importance of such following the use of opioid analgesics as part of the postoperative epidural pain management.

The results of our study are immediately transferable to future candidates for PE surgery at our institution, and with modifications, can be used by other departments offering minimally invasive correction of PE. Our results may also help raise awareness of insufficient pain relief and to explain some of the inter- and intra-individual differences in patients’ response to different opioid analgesics. We consider the study results to be of great value for healthcare personnel responsible for postoperative pain management, especially in the critical transition period from thoracic epidural analgesia to oral analgesia. Using the results of our study as a predicting tool enables surgeons, anaesthesiologists and/or nurses responsible for postoperative pain management to predict expected morphine consumption of the individual patient and to act accordingly. It is possible to establish individual pain management protocols for postoperative pain relief after cessation of thoracic epidural analgesia, either by developing genuine forms of notices or simply by incorporating the regression equation from the multiple linear regression analysis into a computerised spreadsheet with the possibility of entering values for severity of PE, age, weight and type of epidural infusion.

In summary, our study confirmed a linear relationship between preoperative assessment of pectus severity and consumption of opioid analgesics following MIRPE. Thus, postoperative consumption of morphine was increased by 6% (95% CI: 0.3–11%) when preoperative PE depth deteriorated by 1 cm. We conclude that knowledge of pectus severity might be useful to predict the expected morphine consumption in future patients, especially in the critical transition period from epidural analgesia to oral analgesia. However, the considerable variability in the consumption of morphine following MIRPE indicates that the model should be used as a guideline in clinical practice.

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