Cardiology in the Young

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Post-operative vomiting and enhanced recovery after congenital cardiac surgery

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Abstract

Background: Post-operative nausea and vomiting is frequent after congenital cardiac surgery. Aims: We sought to determine factors associated to severe post-operative vomiting after congenital cardiac surgery and the effect on post-operative outcomes. *Methods:* Patients > 30 days of age who underwent elective cardiac surgical repair as part of an enhanced recovery after congenital cardiac surgery programme were retrospectively reviewed. Patient characteristics and perioperative factors were compared by univariate analysis for patients with severe post-operative vomiting, defined as three events or more, and for patients with no-or-mild post-operative vomiting. All variables with a p-value < 0.1 were included in a multivariable model, and major post-operative outcomes were compared using regression analysis. *Results:* From 1 October, 2018 to 30 September, 2019, 430 consecutive patients were included. The median age was 4.8 years (interquartile range 1.2–12.6). Twenty-one per cent of patients (91/430) experienced severe post-operative vomiting. Total intraoperative opioids > 5.0 mg/kg of oral morphine equivalent (adjusted odds ratio 1.72) and post-operative inotropes infusion(s) (adjusted odds ratio 1.64) were identified as independent predictors of severe post-operative vomiting after surgery. Patients suffering from severe post-operative vomiting had increased pulmonary complications (adjusted odds ratio 5.18) and longer post-operative hospitalisation (adjusted coefficient, 0.89). *Conclusions:* Greater cumulative intraoperative opioids are associated with severe post-operative vomiting after congenital cardiac surgery. Multimodal pain strategies targeting the reduction of intraoperative opioids should be considered during congenital cardiac surgery to enhance recovery after surgery.

Post-operative nausea and vomiting occurs frequently in the paediatric population but has seldom been studied in the context of congenital cardiac surgery.[1,2] Vomiting causes patient discomfort and distress after surgery and can delay the ability to resume enteral intake, oral medications, and the discontinuation of intravenous fluids when it occurs repeatedly.[3]

In 2018, we implemented an enhanced recovery after surgery programme in congenital cardiac surgery with the goal to ameliorate surgical outcomes, reduce duration of hospitalisation, and improve patient and family satisfaction. The programme consists of multiple steps or programme components, targeting the reduction of perioperative stress and/or associated with improved outcomes in congenital cardiac surgery (Fig 1). This value-based programme spans the entire surgical period.[4] Recently, this approach has been gaining broad interest in congenital cardiac surgery, and the evidence behind the approach and its major components were reviewed in an expert consensus document spearheaded by the American Association for Thoracic Surgery Congenital Cardiac Surgery Working Group.[5]

In an early review of programme outcomes at our institution, we found an incidence of post-operative vomiting of 50%, despite high adherence to a nausea and vomiting prophylaxis protocol (66% adherence),[4] and it became an area of focus for quality improvement. In children undergoing atrial septal defect closure, a previous study found that age and bypass duration were found to be associated with post-operative vomiting,[2] but the scope of the enhanced recovery programme includes a wider variety of procedures.[4] Therefore, with this analysis, we sought to determine factors associated with severe post-operative vomiting after elective congenital cardiac surgery and the impact on post-operative outcomes in an enhanced recovery programme. We hypothesised that severe post-operative vomiting would be associated with a delay in patient recovery and thus, a longer duration of hospitalisation.

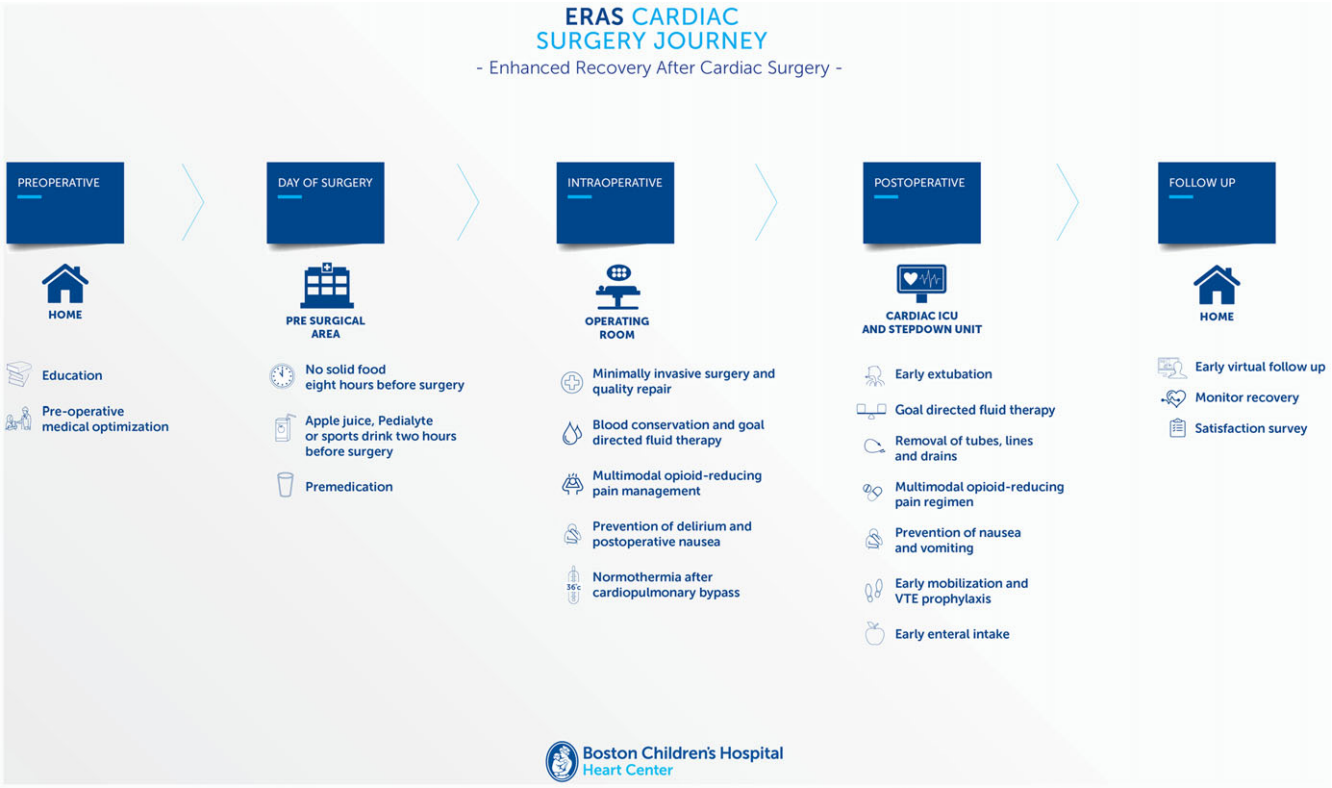

Figure 1. Enhanced recovery after cardiac surgery program at Boston Children's Hospital. Note: All rights reserved, Roy et al. Journal of Thoracic and Cardiovascular Surgery[4].

Materials and methods

Enhanced recovery programme patient selection and data collection

Patients >30 days of age with few comorbidities undergoing elective, low-to-moderate complexity cardiac repairs are eligible for the enhanced recovery after cardiac surgery programme, a quality improvement perioperative initiative at Boston Children's Hospital. This programme consists of a goal-directed evidence-based programme with protocols including early extubation, opioid-sparing multimodal pain regimen, and prophylaxis against post-operative nausea and vomiting.[4]

We retrospectively reviewed data from all patients who underwent elective cardiac surgical repair as part of the cardiac-enhanced recovery programme for the first year of the programme from October, 2018 to September, 2019. The study was approved by the institutional review board (IRB-P00034189). Patient baseline characteristics and intraoperative and perioperative variables were retrieved from the electronic medical record. Opioids were converted into oral morphine equivalents per kilogram using standard conversion factors and reported intraoperatively, and at 24 and 48 hours after surgery.[6] Since young children are often not able to describe nausea, severe post-operative vomiting, defined as three or more episodes of post-operative vomiting, was used as the primary end point.[7,8] Adherence to the enhanced recovery programme components, such as the use of antiemetics prior to extubation, were monitored and obtained from a quality improvement database. Major post-operative outcomes including complications, as defined by the Society for Thoracic Surgery (STS), cardiac reinterventions at 30 days, readmissions at 30-day post-discharge, and length of stay were obtained from the Society for Thoracic Surgery congenital database.

Statistical analysis

Data were presented as frequency (%) for categorical variables and median (interquartile range) for continuous non-normally distributed variables. Patient characteristics and perioperative variables potentially influencing severe post-operative vomiting were evaluated by univariate analysis using Fisher's exact test, the Chi-squared test, or the Wilcoxon rank-sum test for categorical and continuous data, as appropriate. All variables with $p < 0.1$ upon univariate analysis were included in the multivariable analysis, and a multivariable backward elimination model building was implemented with p-removal > 0.2. Logistic regression modelling was used to obtain odds ratios and 95% confidence intervals for severe post-operative vomitting. Receiver operating characteristic curve analysis was implemented to dichotomise intraoperative opioid equivalents, with Youden's J index used to determine the optimal cut-off values by maximising sensitivity and specificity. Results from the receiver operating characteristic analyses were summarised with the area under the curve and corresponding 95% confidence interval. Pearson's correlation was used to analyse the relationship between predictors of severe post-operative vomiting. Multivariable median regression was used to evaluate the association between severe post-operative vomiting and non-normally distributed continuous post-operative outcomes, with results expressed as the adjusted coefficient with 95% confidence intervals. Multivariable logistic regression was used to analyse post-operative complications. Logistic regression results are presented as adjusted

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Table 1. Pre-operative demographics and patient characteristics

Variable	No-or-mild POV (≤2) (N = 339)	Severe POV (≥3) (N = 91)	p-Value
Median age at surgery (years)	5.1 (1.3–12.6)	3.7 (0.9–10.8)	0.310
Infants (< 1-year-old)	78 (23%)	24 (26%)	0.503
ACHD	39 (12%)	11 (12%)	0.877
Male	179 (53%)	52 (58%)	0.461
Median weight for age z-score	−0.4 (−1.5 to 0.5)	−0.7 (−1.6 to 0.1)	0.255
Gastrointestinal condition or previous procedure	23 (7%)	7 (8%)	0.763
Genetic syndrome	52 (15%)	7 (8%)	0.060
Prior cardiac surgery	131 (39%)	39 (43%)	0.465
STAT risk category			0.354
1	116 (34%)	28 (31%)	
2	136 (40%)	38 (42%)	
3	43 (13%)	14 (16%)	
4	40 (12%)	10 (11%)	
5	0 (0%)	1 (1%)	

POV = post-operative vomiting, N = number, ACHD = adults with congenital heart disease, STAT = Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery.
Data are presented as frequency (%) for categorical variables and median (interquartile range: IQR) for continuous non-normally distributed variables.
Fisher's exact test, the Chi-squared test or the Wilcoxon rank-sum test were applied for categorical and continuous data, as appropriate.

odds ratios with 95% confidence intervals. A two-tailed alpha level of 0.05 was used to determine statistical significance. Stata (version 15.0, StataCorp LLC., College Station, Texas) was used to perform all statistical analyses.

Results

A total of 430 patients were enrolled in the enhanced recovery after cardiac surgery programme from 1 October, 2018 to 30 September, 2019. The median age was 4.8 years (interquartile range 1.2–12.6) and 54% (231/430) were male. Demographics and patient characteristics are presented in Table 1. All patients received an inhalational-based anesthetic for maintenance, including during cardiopulmonary bypass. No patients received a total intravenous anesthetic approach. Post-operative vomiting within 24 hours of surgery was observed in 19% (80/430) of patients at a median of 12 hour (interquartile range 7–15) from admission to the ICU. Fifty per cent (211/430) of patients experienced post-operative vomiting, and 21% (91/430) had severe post-operative vomiting (≥ 3 vomiting episodes) at a median of 22 hours (interquartile range 10–56) after admission to the ICU. There were no significant differences in patient characteristics between groups, except for a history of post-operative nausea and vomiting with anesthesia documented at the pre-operative visit: 11/49 (22%) for severe post-operative vomitting versus 21/211 (10%) for no-or-mild vomiting; p = 0.016.

Perioperative variables are presented in Table 2. Twenty-two per cent of the total patient population (94/430) were extubated in the operating room and 72% (308/430) received prophylaxis against nausea and vomiting prior to extubation (either in the operating room and/or in the ICU). There was no difference between patients who experienced severe post-operative vomiting, and no-or-mild vomiting in receiving prophylaxis, or the type of medication(s) used. By univariate analysis, use of ketamine as premedication or during surgery, surgery on cardiopulmonary bypass, cardiopulmonary bypass duration, total intraoperative opioids reported as oral morphine equivalents, longer mechanical ventilation after surgery, and the need for post-operative inotrope infusion(s) were significantly associated with severe post-operative vomiting. There was no significant difference in post-operative opioid utilisation at 24 and 48 hours after surgery between groups. Extubation in the operating room was inversely associated with severe post-operative vomiting, and the patients extubated in the operating room received significantly less intraoperative opioids (median = 2.6 mg/kg of oral morphine equivalents, interquartile range 2.3–3.4) compared to those who were extubated in the ICU (median = 7 mg/kg of oral morphine equivlents, interquartile range 5.2–9.4) ($p < 0.001$).

Total dose of intraoperative opioids was dichotomised using a receiver operating characteristic curve analysis. A cut-off of > 5.0 oral morphine equivalents in mg/kg was determined based on Youden's J index in receiver operating characteristic analysis, with an area under the curve equal to 0.608 (95% CI: 0.546, 0.670) in predicting severe post-operative vomiting.

By multivariable logistic regression analysis, total intraoperative opioids reported as oral morphine equivalents (adjusted OR 1.72; 95% CI: 1.01, 2.92) and the use of post-operative inotrope infusion(s) (adjusted OR 1.64; 95% CI: 1.01, 2.67) were identified as independent predictors for severe post-operative vomiting (Table 3).

When comparing post-operative outcomes after adjusting for inotrope infusion (Table 4), hospital length of stay was significantly longer in patients who had severe post-operative vomiting (median 5.8 days, interquartile range 4.1–8.0) compared to patients with no-or-mild vomiting (median 5.0 days, interquartile range 4.0–6.1) (adjusted coefficient, 0.89; 95% CI: 0.36, 1.42). In addition, patients with severe post-operative vomiting had significantly more pulmonary complications post-operatively (7%, 6/91) compared to patients with no-or-mild vomiting (1%, 4/339), (adjusted OR, 5.18; 95% CI: 1.40, 19.1).

Discussion

Post-operative nausea and vomiting are common in children after surgery,[1,2,9,10] and despite adherence to medical prophylaxis, 50% of patients in our enhanced recovery after cardiac surgery experienced post-operative vomiting. This study found that total intraoperative opioids and the need for post-operative inotrope infusion(s) were independently associated with an increased risk of severe post-operative vomitting. Dopamine was the most frequently used inotrope and was infused post-operatively in 41% of the patients with severe post-operative vomiting. Dopamine receptors may have a role in post-operative nausea and vomitting centrally,[11] but additionally inotropes in the post-operative period may be a marker of reduced cardiac output, hypotension, and higher complexity, and this may impact overall outcomes.[12] After adjusting for inotrope infusion, this study identified that patients experiencing severe post-operative vomiting had longer hospitalisation.

In the enhanced recovery programme, patients who were extubated in the operating room received less intraoperative opioids than those extubated in the ICU and intraoperative extubation was inversely correlated with post-operative vomiting. Historically, the management of pain during cardiac surgery has

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Table 2. Factors associated with severe post-operative vomiting

Risk factor	No-or-mild POV (≤2) (n = 339)	Severe POV (≥3) (n = 91)	p-Value
Pre-operative			
History of PONV	21/211 (10%)	11/49 (22%)	0.016
Fasting time for clear fluids (hrs)	5.3 (1.6–7.4) (N = 145)	4.3 (1.3–5.5) (N = 35)	0.166
Fasting time for solids (hours)	7.4 (5.3–9.6) (N = 282)	6.9 (4.7–8.6) (N = 74)	0.077
Intraoperative			
First blood glucose (mg/dL)	93 (85–103)	92 (83–100)	0.649
Medication			
Ketamine	191 (56%)	62 (68%)	0.042
Midazolam	310 (91%)	81 (89%)	0.473
Total intraoperative opioids (OME; mg/kg)	5.0 (3.2–8.2)	6.2 (4.5–9.1)	0.002
Multimodal pain regimen during anesthesia	307 (91%)	76 (84%)	0.056
IV Acetaminophen	219 (65%)	49 (54%)	0.060
Ropivacaine local/regional	281 (83%)	71 (78%)	0.285
Cardiopulmonary bypass (CPB)	307 (91%)	89 (98%)	0.026
CPB time (min)	84 (55–125)	98 (66–134)	0.045
Aortic clamp time (min)	61 (40–93)	60 (40–93)	0.555
PONV prophylaxis regimen	245 (72%)	63 (69%)	0.568
Ondansetron	214 (63%)	53 (58%)	0.394
Dexamethasone	140 (41%)	36 (40%)	0.765
Scopolamine patch	41 (12%)	7 (8%)	0.236
Duration of anesthesia (min)	356 (300–410)	362 (302–436)	0.275
Duration of surgery (min)	216 (162–268)	216 (175–291)	0.160
Operating room extubation	83 (25%)	11 (12%)	0.011
Post-operative			
Mechanical ventilation (hours)	6.2 (0.2–10.0)	7.5 (4.2–12.3)	0.024
Extubation ≤ 8 hours	212 (63%)	52 (57%)	0.348
Propofol	153 (45%)	44 (48%)	0.584
Dexmedetomidine	148 (44%)	50 (55%)	0.055
Inotropes	105 (31%)	43 (47%)	0.004
Dopamine	90 (27%)	37 (41%)	0.009
Epinephrine	19 (6%)	14 (15%)	0.002
Multimodal pain regimen	339 (100%)	91 (100%)	–
Acetaminophen IV	333 (98%)	89 (98%)	0.679
Ketorolac	299 (88%)	80 (88%)	0.940
OME 24 hours (mg/kg/24 hours)	0.57 (0.30–0.91)	0.60 (0.34–0.93)	0.343
OME 48 hours (mg/kg/24 hours)	1.21 (0.80–1.66)	1.25 (0.90–1.76)	0.392

POV = post-operative vomiting, PONV = post-operative nausea and vomiting, OME = oral morphine equivalent, IV = intravenous, CPB = cardiopulmonary bypass.
Data are presented as frequency (%) for categorical variables and median (interquartile range) for continuous non-normally distributed variables.
Fisher's exact test, the Chi-squared test or the Wilcoxon rank-sum test were applied for categorical and continuous data as appropriate.

been principally controlled by high narcotic doses due to its analgesic and anesthetic effects, as opioids have been demonstrated to reduce the stress response to surgery.[13,14] However, in enhanced recovery programmes, application of protocol-based multimodal anesthesia with limited intraoperative use of respiratory depressant is recommended to enable early, sustained extubation.[5] Multimodal pain regimens including non-opioid medications are effective strategies and decrease opioid use in the post-operative period.[5,15] Furthermore, regional anesthesia techniques have shown their efficacy in children undergoing cardiac surgery and

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Table 3. Multivariable logistic regression analysis for factors associated with severe post-operative vomiting

Variable	Adjusted odds ratio (OR)	95% CI	p-Value
Ketamine	1.44	0.86, 2.40	0.161
Intraoperative opioids (OME/mg/kg) > 5	1.72	1.01, 2.92	0.044
Surgery with cardiopulmonary bypass	2.88	0.65, 12.74	0.164
Post-operative inotropes	1.64	1.01, 2.67	0.048

OR = odds ratio, CI = confidence interval, OME = oral morphine equivalent, mg = milligram, kg = kilogram.
Odds ratios for severe emesis with 95% confidence intervals, and p-values were obtained using multivariable logistic regression modelling with backwards elimination model.

Table 4. Association between severe post-operative vomiting and major post-operative outcomes

Post-operative outcomes	No-or-mild POV (≤2) (n = 339)	Severe POV (≥3) (n = 91)	Adjusted coefficient or odds ratio (OR)	95% CI
ICU LOS (days)	1.1 (0.9–1.9)	1.2 (0.9–2.1)	0.08	−0.01, 0.17
Post-operative LOS (days)	5.0 (4.0–6.1)	5.8 (4.1–8.0)	0.89	0.36, 1.42
All complications	47 (13.9%)	21 (23.1%)	1.60	0.89, 2.90
Arrhythmias	36 (10.6%)	13 (14.3%)	1.13	0.56, 2.29
Pulmonary complications*	4 (1.2%)	6 (6.6%)	5.18	1.40, 19.1

POV = post-operative vomiting; n = number; OR = odds ratio; CI = confidence interval; LOS = length of stay.
*Pulmonary complications are defined by STS: infection, effusion requiring drainage, and pneumothorax.
Data are presented as frequency (%) for categorical variables and median (interquartile range) for continuous non-normally distributed variables.
All models are adjusted for use of inotropes post-operatively.

reduce the need for opioids in the perioperative period.[5,16–19] Emerging studies using superficial blocks, such as bilateral erector spinae, show promise and low risk for complications.[18–20]

In children aged >3 years undergoing non-cardiac surgery, increased duration of anesthesia, type of surgery (strabismus), opioid doses, and a previous anesthetic history of post-operative nausea and vomiting have been reported as risk factors for post-operative nausea and vomiting, and these factors have been incorporated in scoring systems.[9,10] Studies in adult patients undergoing cardiac surgery identified female gender, and a previous anesthetic history of post-operative nausea and vomiting as risk factors.[21–23] Regarding medication prophylaxis, randomised trials demonstrated the effect of intravenous ondansetron or ramosetron in decreasing post-operative nausea and vomiting.[24] Droperidol has also been shown to ameliorate post-operative nausea and vomiting in patients who underwent cardiac surgery,[23] and metoclopramide was found to be more efficacious than ondansetron in a comparative study (24.8% versus 42.6%).[8] Perioperative prophylaxis against nausea and vomiting is a well-adhered protocol and an important step of the enhanced recovery after cardiac surgery at our institution.[4] At 1 year, 72% of patients in the enhanced recovery programme received prophylactic medication against nausea and vomiting prior to extubation, including 42% (180/430) intraoperatively. Metoclopramide use in our institution is low and was only used in 2% (10/430) of the patients, in favour for ondansetron 62% (267/430) and dexamethasone 41% (176/430). Older teenagers and adults may receive a scopolamine patch intraoperatively.[4] As a result of the high level of adherence to the programme protocol, prophylaxis or the choice of medication was not found to be statistically different in preventing post-operative vomiting.

Important limitations include the retrospective nature of this single-centre study and the biases inherent to this type of analysis, which limit generalisability. Furthermore, important factors such as a previous anesthetic history for post-operative nausea and vomiting could not be evaluated in the multivariate model due to the absence of documentation in the medical record from a large number of patients. An additional limitation is that the presence of nausea was not considered in this study, since young children have difficulty reporting it.

In summary, this study demonstrated that severe post-operative vomiting is associated with a longer hospitalisation, and that total dose of intraoperative opioids is independently associated with severe post-operative vomiting after elective congenital cardiac surgery. This study highlights that opioid-sparing strategies in the operating room including adjunct medication and regional techniques, and early extubation are essential components of an enhanced recovery programme. A better understanding of these relationships is also important to improve patient comfort and family satisfaction and to reduce complications and post-operative hospitalisation with this type of quality improvement initiative.

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