

## Supplemental Material

**Table S1.** STROBE Checklist

**Table S2.** Covariates included in the adjusted multivariable model for the impact of gabapentin on subsequent midazolam and morphine requirements

**Table S3.** Gabapentin dosing and prescription practices (n=74)

**Table S4.** Multivariable associations with gabapentin administration

**Table S5.** Demographics based on gabapentin administration on postoperative days 0-4

**Table S6:** Impact of gabapentin administration on postoperative days 0-4 on total morphine and midazolam equivalents requirements on postoperative days 5-7 using linear regression with log-transformation (n=323)

**Table S7:** Impact of gabapentin administration on postoperative days 0-4 on total morphine and midazolam equivalents requirements on postoperative days 5-7 using sub-cohort discharged on postoperative day 5 or later (n=265)

**Figure S1:** Median total doses of different analgesics and sedatives administered in the first 7 postoperative days over time

**Table S1. STROBE Checklist**

	<b>Item No</b>	<b>Recommendation</b>	<b>Page No</b>
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-3
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6-7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	5-6-7
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	7
Outcome data	15*	Report numbers of outcome events or summary measures over time	7

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7-8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8 to 12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

**Table S2:** Covariates included in the adjusted multivariable model evaluating the impact of gabapentin on subsequent benzodiazepines and opiates requirements

Total midazolam equivalent daily dose (mg/kg) on postoperative days 0-4
Total morphine equivalent daily dose (mg/kg) on postoperative days 0-4
Total ketamine daily dose (mg/kg) on postoperative days 0-4
Total dexmedetomidine daily dose (mg/kg) on postoperative days 0-4
Gender
Race
Gestational age
Birth weight
Age at SCPC
Cardiopulmonary bypass time
Any neurologic disorder
Heterotaxy syndrome
Bidirectional Glenn as SCPC procedure
Surgeon identifier
Timing of SCPC <sup>1</sup> (early, middle, late)

<sup>1</sup>Timing of SCPC based on year of operation: early = 2011, 2012 and 2013, middle = 2014, 2015 and 2016, late = 2017, 2018, 2019

SCPC = *superior cavopulmonary connection*

**Table S3:** Gabapentin dosing and prescription practices (n=74)

<b>Starting dose</b>	5.7 mg/kg/day (3.3, 15.0)
<b>Maximum dose</b>	10.7 mg/kg/day (5.5, 23.4)
<b>Time to maximum dose</b>	3.5 days (2.0, 5.2)
<b>Discharged home on medication (n, %)</b>	54/74 (72.9%)

Values are presented as median (IQR) unless otherwise specified

**Table S4:** Multivariable associations with gabapentin administration

<b>Variables</b>	<b>Odds ratio (95% CI)</b>	<b>p-value</b>
<b>Male sex</b>	1.76 (0.91, 3.42)	0.09
<b>Prior Surgery</b>		
None	REFERENCE	-
Norwood	4.48 (0.92, 21.9)	0.06
Shunt only	3.86 (0.75, 19.96)	0.11
Pulmonary artery banding	0.88 (0.10, 7.90)	0.91
Catheterization-based procedure	5.30 (0.63, 44.80)	0.13
<b>Age at SCPC</b>	0.99 (0.99, 1.01)	0.97
<b>Weight at SCPC</b>	0.66 (0.44, 1.00)	0.050
<b>Year at SCPC</b>		
2011	REFERENCE	-
2012	4.02 (0.43, 37.77)	0.22
2013	3.95 (0.45, 34.84)	0.22
2014	0.87 (0.05, 14.96)	0.92
2015	7.30 (0.809, 65.82)	0.08
2016	7.64 (0.88, 66.23)	0.07
2017	20.21 (2.39, 170.98)	0.006
2018	48.23 (5.48, 406.78)	<0.001
2019	25.37 (2.22, 289.98)	0.009

*SCPC: superior cavopulmonary connection*

**Table S5: Demographics based on gabapentin administration on postoperative days 0-4<sup>1</sup>**

	All (N=323)	Gabapentin (N=60)	No Gabapentin (N=263)	p-value <sup>2</sup>
<b>Male (n, %)</b>	198 (61.3)	45 (75.0)	153 (58.2)	0.02
<b>Race (n, %)</b>				0.26
Caucasian	187 (57.8)	39 (65.0)	148 (56.2)	
Black	48 (14.9)	4 (6.7)	44 (16.7)	
Asian and Pacific Islander	9 (2.8)	2 (3.3)	7 (2.7)	
Other	79 (24.5)	15 (25.0)	64 (24.3)	
<b>Gestational Age (weeks)</b>	39 (38, 39)	39 (38, 39)	39 (38, 39)	0.70
<b>Premature<sup>3</sup> (n, %)</b>	29	6 (10.0%)	23 (8.7%)	0.83
<b>Birthweight (kg)</b>	3.20 (2.88, 3.50)	3.20 (2.79, 3.53)	3.18 (2.89, 3.50)	0.99
<b>Chromosomal abnormality (n, %)</b>				0.19
None	313 (96.9)	56 (93.3)	257 (97.7)	
Trisomy 21	2 (0.6)	1 (16.7)	1 (0.4)	
Other	8 (2.5)	3 (5.0)	5 (1.9)	
<b>Major neurologic disorder (n, %)</b>	39	10 (16.7%)	29 (11.0%)	0.23
<b>Heterotaxy syndrome (n, %)</b>	36	3 (5.0%)	33 (12.5%)	0.09
<b>Anatomy (n, %)</b>				0.16
Right ventricle-dominant	174 (53.9)	39 (65.0)	135 (51.3)	
Left ventricle-dominant	99 (30.7)	14 (23.3)	85 (32.3)	
Mixed	50 (15.4)	7 (11.7)	43 (16.3)	
<b>Prior surgery (n, %)</b>				0.04
None	28 (8.7)	2 (3.3)	26 (9.9)	
Norwood operation	179 (55.4)	40 (66.7)	139 (52.9)	
Shunt only	83 (25.7)	13 (21.7)	70 (26.6)	
Pulmonary artery banding	18 (5.5)	1 (1.7)	17 (6.5)	
Catheterization-based procedure	9 (2.7)	4 (6.7)	5 (1.9)	
Other	6 (1.9)	0 (0.0)	6 (22.8)	
<b>Type of SCPC (n, %)</b>				0.73
Unilateral bidirectional Glenn	243 (75.2)	44 (73.3)	199 (75.7)	
Bilateral bidirectional Glenn	36 (11.1)	6 (10.0)	30 (11.4)	
Hemi-Fontan	44 (13.6)	10 (16.7)	34 (12.9)	
<b>Age at SCPC (days)</b>	142 (127, 172)	138.5 (124.5, 161.0)	145 (127.5, 179)	0.039
<b>Weight at SCPC (kg)</b>	6.3 (5.7, 7.0)	6.0 (5.6, 6.9)	6.3 (5.7, 7.0)	0.105
<b>Total CPB (min)</b>	53 (35, 68)	40 (55, 68.5)	53 (34, 68)	0.321
<b>Hospital length of stay (days)</b>	8 (6, 15)	9.5 (7.0, 41.5)	7 (5, 12.5)	<0.0001
<b>CICU length of stay, initial (days)</b>	3.2 (2.1, 5.2)	5.1 (3.0, 11.1)	3.1 (2.1, 5)	0.0001
<b>Year at SCPC</b>				<0.001
2011 <sup>4</sup>	24 (7.4)	1 (1.7)	23 (8.7)	
2012	37 (11.5)	4 (6.7)	33 (12.5)	
2013	59 (18.3)	6 (10)	53 (20.2)	
2014	32 (9.9)	0 (0.0)	32 (12.2)	
2015	35 (10.8)	3 (5.0)	32 (12.2)	
2016	42 (13.0)	6 (10.0)	36 (13.7)	
2017	44 (13.6)	17 (28.3)	27 (10.3)	
2018	40 (12.4)	19 (31.7)	21 (8.0)	
2019 <sup>4</sup>	10 (3.1)	4 (6.7)	6 (2.3)	

<sup>1</sup>Values are presented as median (IQR) unless otherwise specified

<sup>2</sup>P-values from chi-square tests (categorical covariates) or Wilcoxon rank-sum tests (continuous covariates)

<sup>3</sup>Prematurity defined as <37 weeks gestational age

<sup>4</sup>Incomplete data

*CICU = cardiac intensive care unit, CPB = cardiopulmonary bypass, SCPC = superior cavopulmonary connection*

**Table S6:** Impact of gabapentin administration on postoperative days 0-4 on total morphine and midazolam equivalents requirements on postoperative days 5-7 using linear regression with log-transformation (n=323)

	Linear Regression with Log-Transformed Outcome	
	Estimate* (95% CI)	P-value
<b>Total morphine equivalent (mg/kg) on postoperative days 5-7</b>		
Unadjusted effect of gabapentin	0.16 (0.03, 0.30)	0.02
Effect of gabapentin adjusted only for baseline opiates	0.01 (-0.06, 0.11)	0.55
Adjusted effect of gabapentin	0.03 (-0.06, 0.11)	0.55
<b>Total midazolam equivalent (mg/kg) on postoperative days 5-7</b>		
Unadjusted effect of gabapentin	0.04 (-0.05, 0.14)	0.02
Effect of gabapentin adjusted only for baseline benzodiazepines	-0.07 (-0.13, 0.002)	0.06
Adjusted effect of gabapentin	-0.07 (-0.13, -0.01)	0.02

\*Estimates from this model are interpreted as percentage changes

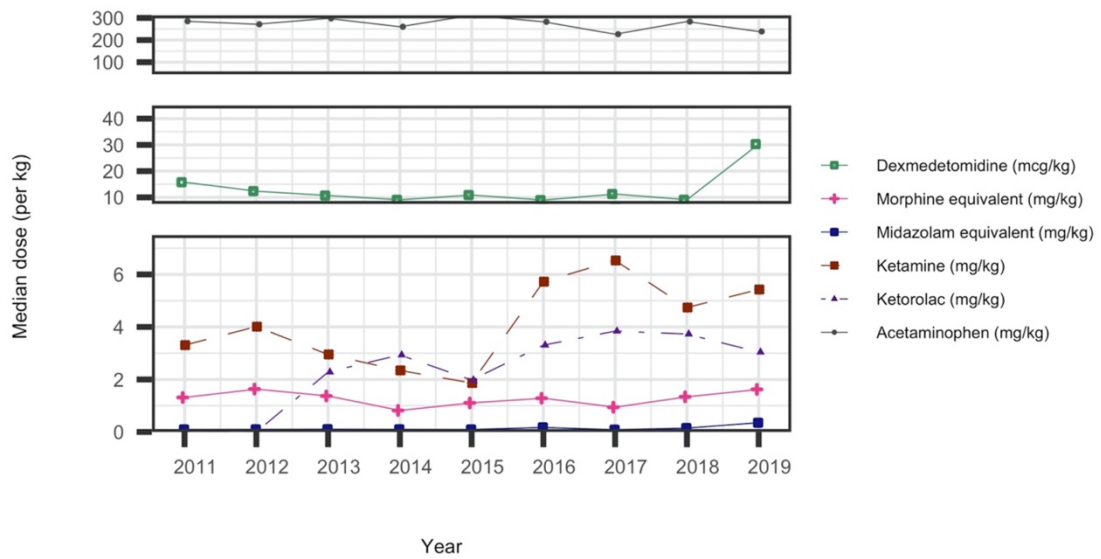


**Table S7:** Impact of gabapentin administration on postoperative days 0-4 on total opiates and benzodiazepine requirements on postoperative days 5-7 using sub-cohort discharged on postoperative day 5 or later (n=265)

	Linear Regression		Linear Regression with Log-Transformed Outcome	
	Estimate (95% CI)	P-value	Estimate* (95% CI)	P-value
<b>Total morphine equivalent (mg/kg) on postoperative days 5-7</b>				
Adjusted effect of gabapentin (multivariable model)	-0.13 (-0.60, 0.34)	0.57	0.01 (-0.08, 0.11)	0.80
<b>Total midazolam equivalent (mg/kg) on postoperative days 5-7</b>				
Adjusted effect of gabapentin (multivariable model)	-0.33 (-0.59, -0.070)	0.01	-0.08 (-0.15, -0.008)	0.03

\*Estimates from this model are interpreted as percentage changes

**Figure S1.** Median total doses of different analgesics and sedatives administered in the first 7 postoperative days over time



*Excluding patients who did not received the medication(s) of interest. Data for 2014 and 2019 are incomplete.*