JPPT | Single Center Retrospective Study

Effect of Dexmedetomidine on Incidence of Hypertension Following Repair of Coarctation of the Aorta

Hope Mae L. Abarintos, PharmD, MAA; Christine A. Kapuscinski, PharmD; Taylor Wheaton, MD; Sierra D. Stauber, PharmD; Michael F. Swartz, PhD; Madeline Grossman, PharmD; Sarah Masri, PharmD; and David J. Hutchinson, PharmD

OBJECTIVE Recent literature suggests a potential role for dexmedetomidine in reducing the incidence and severity of hypertension following repair of coarctation of the aorta (CoA). The primary aim of this study was to assess the association between dexmedetomidine use and the incidence of hypertension following repair of CoA in pediatric patients.

METHODS This was a single-center, retrospective cohort study in patients younger than 19 years who underwent surgical repair of CoA between January 1, 2016, and September 30, 2021. Patients were divided into 2 groups: dexmedetomidine initiation within the first 3 hours after surgery or no dexmedetomidine. The primary outcome was incidence of hypertension within the first 4 to 24 hours after repair. Secondary outcomes included the incidence of hypotension and bradycardia.

RESULTS A total of 80 patients were included, 25 (31.25%) received dexmedetomidine. Median age at the time of procedure was 26 days (IQR, 13–241) in the dexmedetomidine group and 14 days (IQR, 8–53) in the no dexmedetomidine group (p = 0.014). The primary outcome of hypertension was met in 7 patients (28%) in the dexmedetomidine group and 12 patients (21.8%) in the no dexmedetomidine group, p = 0.547. The only variable found to be associated with the incidence of hypertension was age greater than 30 days at the time of procedure. More patients who received dexmedetomidine experienced bradycardia. There was no difference in the incidence of hypotension.

CONCLUSIONS There was no association between the use of dexmedetomidine and the incidence of hypertension following repair of CoA in pediatric patients.

ABBREVIATIONS AAP, American Academy of Pediatrics; CHD, congenital heart disease; CoA, coarctation of the aorta; HR, heart rate; ICU, intensive care unit; JET, junctional ectopic tachycardia

KEYWORDS cardiac; coarctation of the aorta; dexmedetomidine; hypertension; pediatric; surgery

J Pediatr Pharmacol Ther 2024;29(2):144–150

DOI: 10.5863/1551-6776-29.2.144

Introduction

Postoperative hypertension is a common complication following repair of coarctation of the aorta (CoA) in pediatric patients with a reported incidence as high as 70%.[1] Many patients who develop postoperative hypertension will require antihypertensive therapy at discharge. Several mechanisms likely contribute to the development of hypertension following CoA repair and include the adaptation of baroreceptor set points, sympathetic stimulation following resolution of obstruction, and activation of the renin-angiotensin-aldosterone system.[2]

Pharmacologic intervention is often required to maintain normal blood pressure in the immediate postoperative period. Recent literature has identified an emerging role for dexmedetomidine in preventing and treating hypertension following surgical repair of CoA.[3–5] Dexmedetomidine has been theorized to reduce the risk of early postoperative hypertension by decreasing sympathetic output via central α2 adrenergic receptor agonism. Dexmedetomidine use in the pediatric population has increased significantly in recent years because of a growing body of literature supporting the decreased risk of ICU delirium compared with alternative sedative agents, such as opioids and benzodiazepines.[6,7] Dexmedetomidine may provide additional benefits in pediatric patients following cardiac surgery, including decreased incidence of junctional ectopic tachycardia (JET), reduced opioid and benzodiazepine requirements, shorter time to extubation, and decreased length of stay.[2,8–10]

A recent prospective trial of pediatric patients randomized to receive dexmedetomidine or placebo following surgical repair of CoA found that the use of dexmedetomidine reduced the incidence and severity of hypertension.[4] However, the study did not provide

an objective definition of hypertension for comparison in external populations.[4] Further, a case series was published describing the normalization of blood pressure following use of dexmedetomidine in 2 pediatric patients with refractory hypertension after repair of CoA.[3] However, in this limited case series there was no comparison group, and dexmedetomidine was used concomitantly with other antihypertensive treatments. Given these limitations, the clinical application of dexmedetomidine in this population remains uncertain.

The purpose of this study was to assess the association between dexmedetomidine use and the incidence of stage 2 hypertension within the first 24 hours following repair of CoA in pediatric patients. Our study sought to evaluate this outcome using an objective definition for hypertension in an academic medical center that has not been previously described.

Materials and Methods

Patients and Study Design. This was a single-center, retrospective observational study of pediatric patients who underwent surgical repair of CoA at the University of Rochester Medical Center Golisano Children's Hospital. Patients were included if they underwent a primary surgical repair of CoA between January 1, 2016, and September 30, 2021, and were younger than 19 years at the time of the procedure. Use of dexmedetomidine among pediatric patients at our center became significantly more frequent in 2016; thus, the study period was selected to minimize confounding factors related to practice changes over time. Given the fixed sample size, an *a priori* power analysis was not performed.

Patients were excluded if they were initiated on extracorporeal membrane oxygenation or died within the first 24 hours following surgical repair. Patients in whom dexmedetomidine was initiated more than 3 hours after repair were excluded. Our study was designed to examine the effect of dexmedetomidine on the incidence of postoperative hypertension. We therefore sought to compare patients who were initiated on dexmedetomidine early in the postoperative period to those who did not receive dexmedetomidine. Most patients who receive dexmedetomidine for sedation at our center are initiated on dexmedetomidine within the first 3 hours postoperatively, and we therefore considered these patients within the dexmedetomidine group. Those with no documented dexmedetomidine administration within the first 24 hours following repair were placed in the no dexmedetomidine group.

Outcomes. The primary outcome was the incidence of hypertension within the first 4 to 24 hours after surgical repair. Since initiation of dexmedetomidine within the first 3 hours after repair met criteria for inclusion in the dexmedetomidine group, assessing hypertension in the 4 to 24 hours following repair allowed for at least 1-hour time to onset of dexmedetomidine after initiation. All patients underwent continuous heart rate (HR) and blood pressure monitoring via arterial lines. The frequency of HR and blood pressure readings available in the electronic medical record varied from every 15 minutes to hourly. All heart rate and blood pressure measurements available during the study period were included for analysis. Hypertension was defined as 2 consecutive blood pressure measurements at least 15 minutes apart meeting the American Academy of Pediatrics (AAP) definition for stage 2 hypertension, which is: blood pressure greater than or equal to 95th percentile + 12 mm Hg or greater than or equal to 140/90 mm Hg (whichever is lower).[11] Blood pressure targets following repair of CoA vary by institution and are often individualized. Some centers have reported pharmacologic intervention to maintain conservative blood pressures in the early postoperative period.[12] The primary outcome of stage 2 hypertension was chosen by our study investigators in hopes of reducing confounding variables like agitation that can cause a transient or mild increase in blood pressure. We also chose an accepted definition of hypertension to make our outcome data more easily generalizable.

Secondary outcomes included the incidence of bradycardia and hypotension during dexmedetomidine administration and within the first 24 hours after repair. Bradycardia was defined as HR less than the first percentile for age.[13] Hypotension was defined as systolic blood pressure less than 60 mm Hg for those ages 0 to 28 days and less than 70 + (2 × age in years) mm Hg for those older than 28 days. Other outcomes evaluated were the dose and duration of dexmedetomidine administered, incidence of JET, occurrence of antihypertensive medications prescribed during the first 24 hours after repair and at discharge, cumulative doses of benzodiazepines and opioids administered, vasoactive medications administered, and postprocedure and hospital length of stay. Antihypertensive medications evaluated during the 24 hours after procedure and at discharge included captopril, carvedilol, digoxin, enalapril, enalaprilat, esmolol, furosemide, hydralazine, labetalol, losartan, metoprolol, nicardipine, nitroglycerin, propranolol, and valsartan. Vasoactive medications evaluated during the 24 hours after procedure included: epinephrine, milrinone, vasopressin, norepinephrine, dopamine, and dobutamine.

Data Collection. Patients who underwent surgical repair of CoA were identified through locally maintained data as part of the Society of Thoracic Surgeons database and screened for inclusion. Data regarding baseline patient demographics were obtained from the Society of Thoracic Surgeons database, and all other data were collected from the electronic medical record. Data were collected using a standardized case report form developed in REDCap (Research Electronic Data Capture) and a data dictionary.

Data collected included patient demographics, such as age, sex, race/ethnicity, presence of an antenatal diagnosis of congenital heart disease (CHD), and vasoactive-inotropic score. Procedural information, such as urgency of the procedure (e.g., urgent when performed during the initial admission to minimize the chance of further deterioration), surgical approach, length of the procedure, and use of mechanical ventilation in the intensive care unit (ICU), were collected. Medication administration information, including dexmedetomidine administration (dose and duration) within the first 24 hours of repair, use of antihypertensive medications (intermittent or continuous) and inotropic agents within the first 24 hours, and benzodiazepine and opioid medication use (including dose) within the first 24 hours, was collected. Lastly, HR and blood pressure readings via arterial line throughout the initial 24 hours after repair, the incidence of JET, antihypertensive medications prescribed at discharge, and postprocedure and hospital length of stay were collected.

Data Analysis. Demographic characteristics, past medical history, and baseline characteristics were summarized using either medians (IQRs) or means ± SDs for continuous variables, and proportions for categoric variables. Continuous variables were compared using the Mann-Whitney *U* or Student *t*-test and categoric variables using χ^2 analysis or Fisher exact test, as appropriate. Univariable logistic regression was performed to determine the association between dexmedetomidine exposure and the incidence of hypertension. A 2-sided significance level of 0.05 was set for hypothesis testing. All statistics were performed using Stata 16.1 (College Station, Texas).

Results

A total of 87 patients underwent repair of CoA during the study period and were screened. Seven patients were excluded because of missing information or the initiation of dexmedetomidine greater than 3 hours after procedure. Of the 80 patients included in the final analysis, 25 (31.2%) received dexmedetomidine. The median dose of dexmedetomidine administered was 0.5 mcg/kg/hr (IQR, 0.4–0.8) and the median duration of the dexmedetomidine infusion was 17.5 hours (IQR, 9.2–22.3). Patients who received dexmedetomidine were older (median age at the time of procedure was 26 days [IQR, 13–241] vs 14 days [IQR, 8–53], p = 0.014), more likely to undergo a thoracotomy (17 patients [68%] vs 17 patients [30.9%], p = 0.002), and less likely to require mechanical ventilation in the ICU (17 patients [68%] vs 52 patients [94.6%], p = 0.003). Patients who did not receive dexmedetomidine were more likely to have undergone an urgent procedure (15 patients [60%] vs 46 [83.6%], p = 0.021) and to have received a diagnosis of CHD antenatally (3 patients [12%] vs 22 patients [40%], p = 0.011). Complete demographic information is available in Table 1.

The primary outcome of hypertension was met by 7 patients (28%) in the dexmedetomidine group and 12 patients (21.8%) in the no dexmedetomidine group, p = 0.547. We found no significant association between the use of dexmedetomidine and the primary outcome of hypertension (OR, 1.4; 95% CI, 0.5–4.1). Age of 30 days or older and elective procedure were statistically significantly associated with the occurrence of postoperative hypertension in univariable analysis (Table 2). A multivariable analysis was unable to be performed given the small number of cases meeting the primary outcome in the study.

Patients who received dexmedetomidine experienced bradycardia more frequently within 24 hours after procedure, 7 of 25 (28%) vs 1 of 55 (1.8%), p = 0.001. Of the 7 patients in the dexmedetomidine group, 5 experienced bradycardia during the dexmedetomidine infusion. The other 2 patients with documented bradycardia in the dexmedetomidine group experienced bradycardia prior to initiation of dexmedetomidine. During the dexmedetomidine infusion 12 patients (48%) experienced hypotension. There was no difference in hypotension within the first 24 hours after procedure between those who received dexmedetomidine and those who did not, 14 of 25 (56%) vs 33 of 55 (60%), p = 0.755.

Eleven patients (13.8%) received continuous antihypertensive therapy and 9 patients (11.3%) received intermittent antihypertensive therapy (Table 3). The dexmedetomidine group had a higher incidence of requiring a continuous antihypertensive medication compared with those who did not receive dexmedetomidine, 7 of 25 (28%) vs 4 of 55 (7.3%), p = 0.03. There were no differences in the incidence of JET, cumulative doses of benzodiazepines or opioids administered during the first 24 hours after procedure, or antihypertensive medications prescribed at discharge (Table 3). Those who received dexmedetomidine had shorter postprocedure and hospital length of stays (Table 3).

Discussion

In this retrospective observational study of children who underwent surgical repair of CoA, patients who received dexmedetomidine were older and less likely to undergo an urgent procedure or require mechanical ventilation. In this population, we did not find an association between dexmedetomidine exposure and postoperative hypertension. Hypertension was more frequently observed among patients who were older than 30 days at the time of the procedure. This is consistent with previous literature demonstrating patients who undergo CoA repair at an older age are at a higher risk of postoperative hypertension due to longstanding preoperative high blood pressure.[1]

A prospective, randomized controlled trial found that following repair of CoA, patients who received dexmedetomidine had a lower incidence of paradoxical

Table 1. Patient Demographics

Variable	Dexmedetomidine (n = 25)	No Dexmedetomidine (n = 55)	p value
Age at time of procedure, median (IQR), days	26 (13–241)	14 (8–53)	0.014
Age less than 1 yr at time of procedure, n (%)	22 (88)	51 (92.7)	0.671
Sex, n (%)			0.077
Male	18 (72)	28 (50.9)	
Female	7 (28)	27 (49.1)	
Weight, median (IQR), kg	4.3 (3.4–7.2)	3.4 (3.1–4.0)	0.004
Height, median (IQR), cm	56 (50–66)	50 (48–54.5)	0.010
Race/ethnicity, n (%)			0.999
White	24 (96)	47 (85.5)	—
Black	1 (4)	4 (7.3)	—
Hispanic	0 (0)	2 (3.6)	—
Other	0 (0)	2 (3.6)	—
Antenatal diagnosis of CHD, n (%)			0.011
No	22 (88)	31 (56.4)	
Yes	3 (12)	22 (40)	
Unknown	0 (0)	2 (3.6)	
Incision type, n (%)			0.002
Sternotomy	8 (32)	38 (69.1)	—
Thoracotomy	17 (68)	17 (30.9)	—
Mechanical ventilation during ICU admission, n (%)	17 (68)	52 (94.6)	0.003
Urgent/elective procedure, n (%)			0.021
Urgent	15 (60)	46 (83.6)	
Elective	10 (40)	9 (16.4)	

CHD, congenital heart disease; ICU, intensive care unit

hypertension, 9 of 54 (16.7%) vs 20 of 54 (37%).[4] However, patients at our center generally undergo surgical repair of CoA at a younger age compared with the cohort in their study. Given known variability in postoperative management by surgical center and the population-based differences compared with our cohort, it was uncertain if similar effects would be seen in our population. Our study further differed from this previous literature by evaluating the effect of dexmedetomidine on the incidence of hypertension using a discrete definition generated by the AAP given that there was no stated threshold for the primary outcome of hypertension in the abovementioned study.

A reduction in HR is a well-documented side effect of dexmedetomidine recently confirmed in a systemic review and meta-analysis among pediatric cardiac surgery patients.[9] In our study, the incidence of bradycardia did not appear to be associated with a high dose of dexmedetomidine. Among the 5 patients with documented bradycardia while receiving dexmedetomidine, the median dose at the time of bradycardia was 0.4 mcg/kg/hr (IQR, 0.4–0.5) and was similar to the median dose of 0.5 mcg/kg/hr (IQR, 0.4–0.8) received among our entire study population. Our findings align with the results of the meta-analysis that also did not find a correlation between the dose of dexmedetomidine and hemodynamic adverse effects.[9] Notably only 1 of the 5 patients who experienced bradycardia in our study required discontinuation of the dexmedetomidine. All other patients saw resolution without an adjustment in the dexmedetomidine infusion rate. Although the rates of bradycardia observed in our cohort are significant, we feel previously reported literature better describes the adverse effect profile of dexmedetomidine. Therefore, we continue to support the use of dexmedetomidine in pediatric cardiac surgery patients aligning with recently published recommendations.[10]

The use of continuous antihypertensive therapy in our study was higher in the dexmedetomidine group compared with the no dexmedetomidine group. We feel this is largely due to notable differences in the baseline characteristics of our 2 groups. The group that did not receive dexmedetomidine was younger at the time of procedure and therefore less likely to experience postoperative hypertension due to the mechanisms described above. This group was also more likely to undergo an urgent

Table 2. Univariable Analysis of Variables Associated With Hypertension

Variable	Hypertension (n = 19)	No Hypertension (n = 61)	OR (95% CI)	p value
Age at time of procedure, n (%)				
<30 days	6 (31.6)	45 (73.8)	Reference	—
≥30 days	13 (68.4)	16 (26.2)	6.0 (2.0–18.7)	0.002
Antenatal diagnosis of CHD, n (%)*	2 (11.8)	23 (37.7)	0.2 (0.05–1.05)	0.058
Incision type, n (%)				
Sternotomy	10 (52.6)	36 (59.0)	Reference	—
Thoracotomy	9 (47.4)	25 (41.0)	1.3 (0.5–3.6)	0.623
Mechanical ventilation during ICU admission, n (%)	5 (26.3)	10 (16.4)	1.8 (0.5–6.2)	0.338
VIS, median (IQR)†	10 (8–10)	10 (7–10)	1.0 (0.97–1.13)	0.222
Urgent/elective procedure, n (%)				
Urgent	11 (57.9)	50 (82.0)	Reference	—
Elective	8 (42.1)	11 (18.0)	3.3 (1.1–10.1)	0.036
Dexmedetomidine administration, n (%)	7 (36.8)	18 (29.51)	1.4 (0.5–4.1)	0.548
Inotropic agent administration, n (%)	10 (52.6)	41 (67.2)	0.5 (0.2–1.5)	0.252

CHD, congenital heart disease; ICU, intensive care unit; VIS, vasoactive-inotropic score

* Only for the 17 of 19 patients within the hypertension group whom information regarding diagnosis was available.
† Only for those patients (10 of 19 patients within the hypertension group and 41 of 61 within the no hypertension group) who received vasoactive medications.

Table 3. Secondary Outcomes

Characteristic	Dexmedetomidine (n = 25)	No Dexmedetomidine (n = 55)	p value
Bradycardia, n (%)			
During 24 hr after procedure	7 (28)	1 (1.8)	0.001
During dexmedetomidine infusion	5 (20)	—	—
Hypotension, n (%)			
During 24 hr after procedure	14 (56)	33 (60)	0.755
During dexmedetomidine infusion	12 (48)	—	—
Incidence of junctional ectopic tachycardia, n (%)	1 (4)	5 (9.1)	0.66
Antihypertensive therapy administered, n (%)			
Intermittent*	3 (12)	6 (10.9)	0.999
Continuous†	7 (28)	4 (7.3)	0.030
At discharge	12 (48)	32 (58.2)	0.396
Benzodiazepines administered within the first 24 hr, n (%)	4 (4)	21 (38.2)	
Cumulative dose, midazolam, median (IQR), mg/kg	0.38 (0.14–0.57)	0.27 (0.05–0.52)	0.999
Opioids administered within the first 24 hr, n (%)	25 (100)	55 (100)	
Cumulative dose, median (IQR), MME/kg	5.43 (1.4–13)	11.7 (2–23.6)	0.105
Length of stay, median (IQR), days			
After procedure	5 (4–8)	11 (6–23)	0.003
Hospital	7 (4–10)	16 (9–31)	0.003

MME, morphine milligram equivalents

* Six patients received metoprolol, 1 patient labetalol, and 2 patients received both agents.
† Ten patients received nitroprusside, 1 patient received nicardipine.

(vs elective) procedure and to require mechanical ventilation postoperatively, indicating a higher acuity of illness. At our center, it is common to optimize the use of a single sedative agent prior to initiating a second agent. In patients who require postoperative mechanical ventilation, opioids, such as fentanyl and morphine, are frequently used as the first-line therapy. Thus, we suspect dexmedetomidine may have been preferentially prescribed in patients based on their age, lesser acuity of illness, and anticipated duration of mechanical ventilation. There is a lack of evidence-based guidance regarding best practices for the treatment of hypertension after repair of CoA, with significant variability in practice.[5] Most of the patients in our study who required continuous antihypertensive therapy in the early postoperative period received nitroprusside. The predominant use of nitroprusside for continuous antihypertensive therapy in this population is consistent with a multicenter study of 1636 patients after CoA repair in which nitroprusside was used in 86.4% of patients.[5] Adjunctive antihypertensive therapy in our study also included nicardipine, labetalol, and metoprolol.

A strength of our study is that we assessed the effect of dexmedetomidine on hypertension using a discrete blood pressure definition from the AAP. Although the blood pressure threshold associated with adverse outcomes following repair of CoA is poorly defined, the objective definition will allow readers to compare our findings to related literature, their own patient populations, and be used for comparison in future study design and research. Some limitations of our study are related to the retrospective nature. Our study groups had significant differences at baseline, most notably patient age, the need for postoperative mechanical ventilation, and having undergone an urgent versus elective procedure. Although it is possible changes in clinical practice occurred throughout the study period, the multidisciplinary group of investigators is not aware of significant changes likely to have affected the outcomes of our study. Our study is inclusive of the COVID-19 pandemic, which may have affected care during this time. Some data points were incompletely documented in the medical record. There was also variability in the frequency of documentation of blood pressure measurements, ranging from every 15 to every 60 minutes. Therefore, it is possible patients could have experienced hypertension not captured. Another limitation of our study is the small sample size, increasing the likelihood of type II error.

In our study there was no association between the use of dexmedetomidine and the incidence of hypertension following repair of CoA in pediatric patients. Age greater than 30 days at the time of procedure was the only patient-specific factor associated with the incidence of hypertension. The rates of adverse effects seen in our study were similar to those previously reported. Although it is not our current practice to use dexmedetomidine with the goal of preventing postoperative hypertension we continue to use dexmedetomidine for many patients in this population given well-established efficacy and safety as a sedative agent.[10] Future studies evaluating the role of dexmedetomidine in the prevention and treatment of hypertension following repair of CoA may be warranted. Enrolling a larger patient population through a multicenter design and including a controlled comparison group may be necessary to assess relevant outcomes and control for patient confounders.

Conclusion

We observed no association between dexmedetomidine use and the incidence of hypertension following repair of CoA in pediatric patients. Further investigation into the role of dexmedetomidine following repair of CoA is needed.

Article Information

Affiliations. Department of Pharmacy (HLA, CAK, SS, DJH), University of Rochester Medical Center, Rochester, NY; Department of Pediatrics (TW), University of Rochester Medical Center, Rochester, NY; Department of Surgery (MFS), University of Rochester Medical Center, Rochester, NY; Department of Pharmacy Practice and Education (MG, SM, DJH), Wegmans School of Pharmacy, St John Fisher College, Rochester, NY.

Correspondence. Hope Mae L. Abarintos, PharmD, MAA; hopemae_abarintos@urmc.rochester.edu

Disclosure. The authors declare no conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria. The authors had full access to all the data and take responsibility for the integrity and the accuracy of the data analysis.

Ethical Approval and Informed Consent. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and have been approved by the appropriate committees at the University of Rochester Medical Center. However, given the nature of this study (retrospective data collection), informed consent was not required.

Acknowledgments. The authors acknowledge Nicole M. Acquisto for their assistance with manuscript preparation. Preliminary results were presented at Pediatric Pharmacy Association (PPA) Annual Meeting Resident Research Project Showcase virtually on May 5, 2022; and at the Eastern States Regional Residency Meeting virtually on May 16, 2022.

Submitted. February 22, 2023

Accepted. August 21, 2023

References

1. Panzer J, Bové T, Vandekerckhove K, De Wolf D. Hypertension after coarctation repair-a systematic review. *Transl Pediatr*. 2022;11(2):270–279.
2. Roeleveld PP, Zwijsen EG. Treatment strategies for paradoxical hypertension following surgical correction of coarctation of the aorta in children. *World J Pediatr Congenit Heart Surg*. 2017;8(3):321–331.
3. Sahu MK, Manikala VK, Singh SP, et al. Use of dexmedetomidine as an adjunct in the treatment of paradoxical hypertension after surgical repair of coarctation of the aorta in infants. *Ann Card Anaesth*. 2015;18(3):437–440.
4. Soliman R, Saad D. Assessment the effect of dexmedetomidine on incidence of paradoxical hypertension after surgical repair of aortic coarctation in pediatric patients. *Ann Card Anaesth*. 2018;21(1):26–33.
5. Moffett BS, Penny DJ. Variability in treatment of postcoarctectomy hypertension: a multicenter study. *Pediatr Cardiol*. 2016;37(4):772–777.
6. Kiski D, Malec E, Schmidt C. Use of dexmedetomidine in pediatric cardiac anesthesia. *Curr Opin Anaesthesiol*. 2019;32(3):334–342.
7. Schwartz LI, Twite M, Gulack B, et al. The perioperative use of dexmedetomidine in pediatric patients with congenital heart disease: an analysis from the Congenital Cardiac Anesthesia Society-Society of Thoracic Surgeons congenital heart disease database. *Anesth Analg*. 2016;123(3):715–721.
8. Gan L, Zhao X, Chen X. The safety and efficacy evaluation of dexmedetomidine for procedural sedation and postoperative behaviors in pediatric populations: a systematic review and meta-analysis. *Ann Pharmacother*. 2022;56(1):16–26.
9. Wang Q, Chen C, Wang L. Efficacy and safety of dexmedetomidine in maintaining hemodynamic stability in pediatric cardiac surgery: a systematic review and meta-analysis. *J Pediatr (Rio J)*. 2022;98(1):15–25.
10. Smith HAB, Besunder JB, Betters KA, et al. 2022 Society of Critical Care Medicine clinical practice guidelines on prevention and management of pain, agitation, neuromuscular blockade, and delirium in critically ill pediatric patients with consideration of the ICU environment and early mobility. *Pediatr Crit Care Med*. 2022;23(2):e74–e110.
11. Flynn JT, Kaelber DC, Baker-Smith CM, et al; Subcommittee on Screening and Management of High Blood Pressure in Children. *Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics*. 2017;140(3):e20171904.
12. Siersma C, Brouwer CNM, Sojak V, et al. Treatment of post-coarctectomy hypertension with labetalol—a 9-year single-center experience. *World J Pediatr Congenit Heart Surg*. 2022;13(6):701–706.
13. Bonafide CP, Brady PW, Keren R, et al. Development of heart and respiratory rate percentile curves for hospitalized children. *Pediatrics*. 2013;131(4):e1150–e1157.