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The Hemodynamic Response to Dexmedetomidine Loading Dose in Children With and Without Pulmonary Hypertension

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Attestation: Robert H. Friesen attests to the integrity of the original data and the analysis reported in the manuscript and approved the final manuscript.

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Abstract

BACKGROUND—Dexmedetomidine, an α_2 receptor agonist, is widely used in children with cardiac disease. Significant hemodynamic responses, including systemic and pulmonary vasoconstriction, have been reported after dexmedetomidine administration. Our primary goal of this prospective, observational study was to quantify the effects of dexmedetomidine initial loading doses on mean pulmonary artery pressure (PAP) in children with and without pulmonary hypertension.

METHODS—Subjects were children undergoing cardiac catheterization for either routine surveillance after cardiac transplantation ($n = 21$) or pulmonary hypertension studies ($n = 21$). After anesthetic induction with sevoflurane and tracheal intubation, sevoflurane was discontinued and anesthesia was maintained with midazolam 0.1 mg/kg IV (or 0.5 mg/kg orally preoperatively) and remifentanyl IV infusion 0.5 to 0.8 $\mu\text{g/kg/min}$. Ventilation was mechanically controlled to maintain Pco_2 35 to 40 mm Hg. When end-tidal sevoflurane was 0% and fraction of inspired oxygen (Fio_2) was 0.21, baseline heart rate, mean arterial blood pressure, PAP, right atrial pressure, pulmonary artery occlusion pressure, right ventricular end-diastolic pressure, cardiac output, and arterial blood gases were measured, and indexed systemic vascular resistance, indexed pulmonary vascular resistance, and cardiac index were calculated. Each subject then received a 10-minute infusion of dexmedetomidine of 1 $\mu\text{g/kg}$, 0.75 $\mu\text{g/kg}$, or 0.5 $\mu\text{g/kg}$. Measurements and calculations were repeated at the conclusion of the infusion.

RESULTS—Most hemodynamic responses were similar in children with and without pulmonary hypertension. Heart rate decreased significantly, and mean arterial blood pressure and indexed systemic vascular resistance increased significantly. Cardiac index did not change. A small, statistically significant increase in PAP was observed in transplant patients but not in subjects with pulmonary hypertension. Changes in indexed pulmonary vascular resistance were not significant.

CONCLUSION—Dexmedetomidine initial loading doses were associated with significant systemic vasoconstriction and hypertension, but a similar response was not observed in the pulmonary vasculature, even in children with pulmonary hypertension. Dexmedetomidine does not appear to be contraindicated in children with pulmonary hypertension.

The pulmonary vascular effects of many anesthetic drugs have been inadequately investigated. The lack of knowledge of these effects can create uncertainty in the delivery of clinical anesthetic care, particularly in children with congenital heart disease and/or pulmonary hypertension, who frequently require anesthesia or sedation for diagnostic or therapeutic procedures.

Dexmedetomidine, an α_2 and imidazole receptor agonist, is widely used in pediatrics for procedural and therapeutic sedation and as a component of surgical anesthesia. Experience with dexmedetomidine in children with congenital heart disease is growing.^{1–6} A cardiac catheterization study of children with transplanted hearts demonstrated a significant but

transient increase in pulmonary artery pressure (PAP) in response to dexmedetomidine bolus,⁷ but studies of its hemodynamic effects in children with pulmonary hypertension are lacking. The purpose of this study was to document the pulmonary vascular hemodynamic effects of dexmedetomidine in children with and without pulmonary hypertension undergoing cardiac catheterization.

METHODS

This prospective descriptive study was approved by the hospital's IRB. Written informed consent was obtained from the parents or guardians of the subjects, and written assent was obtained from children aged 7 years or older. Subjects were included if they were between 1 and 14 years of age and were scheduled to undergo elective cardiac catheterization for either postcardiac transplant surveillance or periodic pulmonary hypertension assessment. Pulmonary hypertensive subjects were patients known to have pulmonary hypertension (mean PAP pressure >25 mm Hg) documented by prior cardiac catheterization and/or current echocardiographic study. Subjects were approached for enrollment consecutively until 21 transplant subjects and 21 pulmonary hypertensive subjects were studied. Patients were excluded from participation if hemodynamic instability was present, such as in acute rejection or newly diagnosed untreated pulmonary hypertension.

Anesthetic induction was achieved with sevoflurane in oxygen and air. After induction, a peripheral IV catheter was inserted. Infusion of remifentanyl 0.7 µg/kg/min was started, and rocuronium 1 mg/kg was administered. All subjects received midazolam, either 0.5 mg/kg orally pre-operatively or 0.1 mg/kg IV during induction. Five minutes after beginning remifentanyl infusion, the trachea was intubated and pressure-controlled mechanical ventilation was instituted to achieve a tidal volume of 8 mL/kg, positive end-expiratory pressure of 4 cm H₂O, and a respiratory rate sufficient to maintain end-tidal Pco₂ 35 to 40 mm Hg. After intubation, sevoflurane was discontinued and the remifentanyl infusion was maintained at 0.5 to 0.7 µg/kg/min.

After administering 0.5% lidocaine subcutaneously, the cardiologist inserted vascular sheaths in the femoral vein and femoral artery. Baseline hemodynamic measurements were obtained using a transvenous Swan-Ganz catheter (Edwards Lifesciences, Irvine, CA) in fraction of inspired oxygen (Fio₂) of 0.21 (or subject's usual Fio₂ if treated with oxygen preoperatively) after sevoflurane had been discontinued for at least 20 minutes (usually longer) and end-tidal sevoflurane concentration was zero. Hemodynamic data were recorded on the Philips Witt Hemodynamic System (Philips Corporation, Melbourne, FL). Measurements included heart rate (HR), mean arterial blood pressure (MAP), right atrial pressure (RAP), mean PAP, pulmonary artery occlusion pressure (PAOP), right ventricular end-diastolic pressure (RVEDP), cardiac output (by triplicate thermodilution in subjects without intracardiac shunts; by Fick method with oxygen consumption assumed by the LaFarge equation in subjects with intracardiac shunts), Pao₂, Paco₂, arterial pH, blood oxyhemoglobin saturation (Spo₂), and end-tidal Pco₂ (PETCO₂). Calculations of cardiac index (CI), indexed systemic vascular resistance (SVRI), and indexed pulmonary vascular resistance (PVRI) were made using standard formulae.

After baseline measurements were obtained, an initial loading dose of dexmedetomidine 1 µg/kg was administered IV over 10 minutes to the first 7 subjects undergoing transplant surveillance catheterizations. An initial loading dose of 0.75 µg/kg was administered over 10 minutes to the next 7 subjects, and an initial loading dose of 0.5 µg/kg was administered over 10 minutes to the final 7 subjects. All loading doses were followed by continuous infusion of dexmedetomidine 0.7 µg/kg/h. As soon as the 10-minute initial loading dose was complete, hemodynamic measurements as described above were repeated. At this point, the

study was complete, and the anesthetic for the remainder of the procedure (angiograms, biopsies) was managed at the discretion of the anesthesiologist.

In subjects undergoing pulmonary hypertension studies, the baseline measurements were followed by measurements in Fio_2 of 1.0 and, in most cases, during inhaled nitric oxide 40 ppm. Then oxygen and nitric oxide were discontinued, and subjects were allowed to return to baseline condition (MAP and PAP $\pm 5\%$ of baseline values). Dexmedetomidine loading doses were then administered over 10 minutes to subjects in the sequence described for the transplant subjects above. When the loading dose was complete, dexmedetomidine was infused at 0.7 $\mu\text{g/kg/h}$, and hemodynamic measurements were obtained as described above.

Statistical Analysis

Using change in PAP from baseline as the primary outcome, sample size calculation was based on a previous study of the effect of 1 $\mu\text{g/kg}$ dexmedetomidine administered over 10 minutes to adults.⁸ Mean PAP changed from 38.5 ± 11.3 to 25.4 ± 9.4 , which was a 34% change. Using a conservative estimate of the standard deviation (SD) for the difference $\sqrt{2} \times 11.3 = 16$, this difference represents an effect size of 0.82, which is defined as the mean difference divided by the SD of the individual difference. For the current study, we did not want to miss statistical significance if the effect size was as much as 0.48 (which corresponds to about 20% mean difference). In this case, a sample size of 37 was required to ensure 80% power at 5% significance for detecting the difference from baseline using a 2-tailed paired t test. (Another article, published after initiation of our study, reported the effect of a rapid bolus of 0.5 $\mu\text{g/kg}$ dexmedetomidine on PAP and pulmonary vascular resistance (PVR) in children.⁷ Using similar methodology, a sample size of 15 subjects was calculated to demonstrate an effect size of 0.80 with 80% power at 5% significance.)

Statistical analyses were performed using JMP Pro 10 software (SAS, Cary, NC). Each outcome variable was examined for normality of distribution using the Shapiro-Wilk W test. Patient demographic values were normally distributed; they were described using descriptive measures and compared between diagnosis groups using unmatched t tests. Descriptive measures were used to present the severity of pulmonary hypertension and the range of chronic pulmonary vasodilator medications. Blood gas variables were normally distributed, and their changes were analyzed using repeated measures analysis of variance. Changes in normally distributed hemodynamic variables (HR, MAP, RAP, SVRI, PAOP, and RVEDP) from baseline to after dexmedetomidine were analyzed using the paired t test. Similar changes in nonnormally distributed hemodynamic variables (CI, PAP, PVRI, and PVRI/SVRI) were analyzed with the sign rank test. When comparing percentage changes in hemodynamic variables among the 3 dexmedetomidine dosage groups, 1-way analysis of variance was used for normally distributed variables (percentage change HR, MAP, CI, SVRI, PAP, PVRI/SVRI, RVEDP), and the Kruskal-Wallis test was used for nonnormally distributed variables (percentage change RAP, PAOP, and PVRI). The durations that MAP exceeded 10% of baseline after the 3 dexmedetomidine loading doses were compared using 1-way analysis of variance. Descriptive measures were used to describe the extent of pulmonary vascular reactivity to oxygen and nitric oxide. $P < 0.01$ was considered to be statistically significant.

RESULTS

Forty-five subjects were enrolled. The study was not performed in 3 subjects due to hemodynamic instability before administration of dexmedetomidine (1 had a slow junctional rhythm at baseline, 1 was experiencing acute organ rejection, and 1 experienced an acute pulmonary hypertensive exacerbation associated with difficult ventilation during induction of anesthesia). Demographics of the 42 studied subjects are shown in Table 1. Etiologies of

pulmonary hypertension in those 21 subjects included idiopathic ($n = 7$), congenital heart disease ($n = 9$, all 2 ventricle circulations, postsurgical repair, 4 with residual intracardiac shunts), and chronic lung disease ($n = 5$). The severity of pulmonary hypertension and the chronic pulmonary vasodilating medications among pulmonary hypertension subjects are displayed in Table 2. Seventeen pulmonary hypertension subjects were treated with chronic pulmonary vasodilator medications, most with more than 1 drug. Blood gases were stable and unchanged during the study (Table 3).

Hemodynamic responses to dexmedetomidine in the subject groups are displayed in Tables 4 and 5. A statistically significant, clinically mild increase in PAP was observed in heart transplant subjects but not in subjects with pulmonary hypertension. Changes in PVRI were not significant. In both groups, HR decreased significantly, and MAP, SVRI, and RAP increased significantly.

The percentage changes in hemodynamic variables were not significantly different between the 2 subject groups, so the groups were combined to analyze changes by dexmedetomidine dose. Table 6 displays hemodynamic measurements in response to the 3 dexmedetomidine doses. Changes in systemic measurements (HR, MAP, SVRI, RAP) were generally statistically significant after all doses, while changes in pulmonary hemodynamics (PAP, PVRI) were generally insignificant.

Figure 1 displays hemodynamic responses of the entire cohort to the 3 dexmedetomidine doses expressed in percentage change. Changes in MAP were significantly different among dose groups. An increase in MAP $>20\%$ of baseline was observed in 12 of 14 subjects after 1 $\mu\text{g/kg}$ dexmedetomidine and in 11 of 14 subjects after 0.75 $\mu\text{g/kg}$ dexmedetomidine, but in only 3 of 14 subjects after 0.5 $\mu\text{g/kg}$ dexmedetomidine. The duration that MAP exceeded 10% of baseline was significantly different ($P < 0.01$) among dose groups: 14 [5–49] (median [range]) minutes after 0.5 $\mu\text{g/kg}$ dexmedetomidine, 29 [5–95] minutes after 0.75 $\mu\text{g/kg}$, and 39 [7–80] minutes after 1 $\mu\text{g/kg}$.

Subjects with pulmonary hypertension demonstrated pulmonary vascular reactivity before dexmedetomidine infusion: the maximum decrease in PVRI was $44\% \pm 24\%$ (mean $\pm$ SD; range 11%–85%) from baseline when ventilated with 100% oxygen with or without 40 ppm nitric oxide.

DISCUSSION

The results of our study demonstrate that the pulmonary vasculature of children with and without pulmonary hypertension does not respond with significant vasoconstriction to initial loading doses of dexmedetomidine. Although significant increases in MAP and SVRI were observed, the changes in PAP and PVRI were insignificant. This combination of hemodynamic responses should lead to maintenance of coronary perfusion pressure without an increase in right ventricular afterload, suggesting that administration of a dexmedetomidine initial loading dose to children with pulmonary hypertension is acceptable.

Results of studies of pulmonary hemodynamics in response to dexmedetomidine are inconsistent in adults, where dexmedetomidine, in various doses and conditions, has been associated with decreased PAP and unchanged PVR,⁸ increased PAP and PVR,⁹ and unchanged PVR.¹⁰

A pediatric study of the pulmonary hemodynamic effects of dexmedetomidine used transthoracic echocardiography to estimate PAP. After initial loading doses of 0.5 to 1.0 $\mu\text{g/kg}$, a 20% decrease in estimated PAP and no change in ventricular function were

observed.¹¹ Another study examined the hemodynamic effects of a rapid (5 seconds) bolus of either 0.25 or 0.5 µg/kg dexmedetomidine to children undergoing transplant surveillance cardiac catheterizations.⁷ Transient increases in systemic blood pressure and systemic vascular resistance (SVR) were observed at 1 minute and resolved at 5 minutes. Similar but less pronounced changes in PAP and PVR were observed, and PVR/SVR decreased slightly. Our findings are consistent with those results. There have been no previous studies in children with pulmonary hypertension.

The systemic vascular responses that we observed after dexmedetomidine are consistent with prior reports. Although α_2 agonists have central sympatholytic effects and are often used to treat hypertension, a transient systemic hypertensive response has been observed in patients after dexmedetomidine administration.^{7,12} The mechanism for this response is stimulation of vasoconstrictor post-synaptic α_2 receptors in the peripheral vasculature.¹³ Our observation that PVRI remained unchanged while SVRI increased suggests that such vasoconstrictor receptors are not active in the pulmonary vasculature.

Although the denervated transplanted heart might theoretically be less responsive to the central sympatholytic effects of dexmedetomidine, as well as to unopposed or reflex vagal tone, we observed similar hemodynamic responses in our 2 subject groups. Thus, postsynaptic peripheral vaso-constriction is the predominant initial hemodynamic effect of dexmedetomidine initial loading doses.

The statistically significant increases that we observed in RAP, PAOP, and RVEDP did not have apparent clinical importance. We did not observe a significant change in CI, and other studies have demonstrated either no change⁷ or a significant decrease in CI in subjects receiving dexmedetomidine in various dosing regimens.^{8,9,14} These findings suggest that high doses of dexmedetomidine should be given with caution in patients with impaired ventricular function.

One reason that pediatric studies of the hemodynamic effects of anesthetic drugs are limited is that the invasive monitors required to measure pulmonary artery flow and PAP cannot be inserted in the awake subject. Thus, baseline measurements before administration of a study drug must be made in the presence of another anesthetic or sedative. If the baseline anesthetic exerts pulmonary vascular effects, it may be difficult to draw conclusions about the study drug. We chose the combination of remifentanyl and midazolam to provide baseline anesthesia because of their lack of significant pulmonary hemodynamic effects. Although high-dose fentanyl can attenuate pulmonary vasoconstriction in response to noxious tracheal stimulation,¹⁵ opioids have minimal direct hemodynamic effects. PVR remained unchanged in response to fentanyl in children with congenital heart disease,¹⁶ and pulmonary vascular responses to remifentanyl were clinically insignificant in adults with artificial hearts.¹⁷ Midazolam exerted clinically insignificant effects on the pulmonary vasculature of adults with cardiac disease.¹⁸ We believe that the anesthetic used for baseline conditions in our study is one that can appropriately be used for future studies of pulmonary hemodynamics in children.

We present the data on reactivity of PVRI to oxygen and nitric oxide to demonstrate that pulmonary vascular reactivity was present in our subjects with pulmonary hypertension. Patients with fixed, nonreactive pulmonary hypertension who do not react with pulmonary vasodilation in response to oxygen may not react with pulmonary vasoconstriction in response to an appropriate stimulus. A study of children with high-altitude pulmonary edema demonstrated that those who exhibited a vasodilation response to oxygen and nitric oxide also exhibited a vaso-constriction response to hypoxia,¹⁹ so we presume that our

subjects with pulmonary hypertension retained the ability to respond to vasoconstrictive stimuli.

A limitation of our study is that all subjects with pulmonary hypertension were receiving chronic pulmonary vasodilator medications, including prostacyclin analogs, phosphodiesterase inhibitors, endothelin receptor antagonists, and/or calcium channel blockers. This is notable because such therapy has been shown to significantly reduce the risk of cardiovascular complications during anesthesia in children with pulmonary hypertension.²⁰ Thus, we assume that this chronic therapy might have blunted any pulmonary vasoconstrictive effects of dexmedetomidine.

Another limitation is that only the effects of initial loading doses of dexmedetomidine were studied. Time and procedural constraints in this clinical setting precluded the opportunity to obtain further hemodynamic measurements at longer intervals.

We conclude that despite a significant systemic vaso-constrictive response to dexmedetomidine initial loading doses, the pulmonary vasculature does not exhibit a similar response, even in children with pulmonary hypertension. Dexmedetomidine appears to be a reasonable choice for sedation of children with pulmonary hypertension receiving chronic pulmonary vasodilator therapy.

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Figure 1.

Hemodynamic percentage changes after 3 initial loading doses of dexmedetomidine in all 42 subjects. HR = heart rate; MAP = mean arterial blood pressure; PAP = mean pulmonary artery pressure; PVRI = indexed pulmonary vascular resistance; SVRI = indexed systemic vascular resistance; CI = cardiac index; PAOP = pulmonary artery occlusion pressure; RAP = right atrial pressure; RVEDP = right ventricular end-diastolic pressure. Changes in MAP were significantly different among the 3 doses ($P = 0.0025$ by 1-way analysis of variance or Kruskal-Wallis test).

Table 1

Subject Demographics

	PAH	OHT
Age (y)	6.7 ± 3.8	7.6 ± 3.3
Weight (kg)	22 ± 13	25 ± 10
Body surface area (m ²)	0.81 ± 0.33	0.90 ± 0.26

Data are expressed as mean ± SD. $n = 21$ in each group.

Differences are not significant by unpaired t test.

PAH = pulmonary arterial hypertension; OHT = orthotopic heart transplant.

Table 2**Severity and Medications of 21 Pulmonary Hypertension Subjects**

PAH severity by pressure ratio	<i>n</i>	PAP/MAP
Subsystemic (PAP/MAP <0.7)	17	0.43 (0.32–0.54)
Systemic (PAP/MAP = 0.7–1.0)	4	0.82 (0.78–0.86)
Suprasystemic (PAP/MAP >1.0)	0	
PAH severity by resistance ratio	<i>n</i>	PVRI/SVRI
PVRI/SVRI <0.25	6	0.17 (0.13–0.20)
PVRI/SVRI = 0.25–0.5	11	0.35 (0.33–0.44)
PVRI/SVRI >0.5	4	0.74 (0.58–0.84)
Chronic pulmonary vasodilator medications	<i>n</i>	
Phosphodiesterase inhibitors	17	
Endothelin receptor antagonists	10	
Prostacyclin analogs	4	
Calcium channel blockers	4	
None	4	

Data are expressed as median (interquartile range).

PAH = pulmonary arterial hypertension; PAP = mean pulmonary artery pressure; MAP = mean arterial blood pressure; PVRI = indexed pulmonary vascular resistance; SVRI = indexed systemic vascular resistance.

Table 3**Blood Gas Data**

	PAH		OHT	
	Baseline	Dexmedetomidine	Baseline	Dexmedetomidine
Pao ₂ (mm Hg)	66 ± 10	64 ± 11	76 ± 9	76 ± 8
Paco ₂ (mm Hg)	36 ± 4	38 ± 5	36 ± 3	36 ± 2
pH	7.38 ± 0.03	7.38 ± 0.03	7.36 ± 0.04	7.36 ± 0.04
SpO ₂ (%)	93 ± 3	92 ± 3	94 ± 3	95 ± 3
PETCO ₂ (mm Hg)	36 ± 2	35 ± 8	37 ± 1	37 ± 2

Data are expressed as mean ± SD. *n* = 21 in each group.

Differences are not significant by repeated measures analysis of variance.

PAH = pulmonary arterial hypertension; OHT = orthotopic heart transplant.

Table 4**Hemodynamic Measurements in Children with Pulmonary Hypertension**

	Baseline	Dexmedetomidine	Change (99% confidence interval)	P
HR (bpm)	86 ± 15	77 ± 1	−9 (−15 to −4)	0.0001
MAP (mm Hg)	57 ± 6	72 ± 13	15 (8 to 22)	<0.0001
RAP (mm Hg)	6 ± 2	7 ± 2	1.6 (0.7 to 2.4)	<0.0001
CI (L/min/m ²)	3.4 ± 0.5	3.3 ± 0.7	0 (−0.4 to 0.3)	0.8238
SVRI (Wood u × m ²)	15.2 ± 2.5	19.5 ± 5.5	4.4 (1.6 to 7.1)	0.0002
PAP (mm Hg)	28 ± 11	30 ± 9	1.5 (−1.8 to 4.8)	0.2146
PVRI (Wood u × m ²)	5.6 ± 2.7	5.6 ± 2.0	−0.1 (−1.1 to 1.0)	0.8593
PVRI/SVRI	0.38 ± 0.21	0.30 ± 0.13	−0.08 (−0.16 to 0)	0.0104
PAOP (mm Hg)	8 ± 2	9 ± 3	1.4 (−0.1 to 2.9)	0.0136
RVEDP (mm Hg)	7 ± 2	9 ± 2	1.7 (0.7 to 2.8)	0.0002

Data expressed as mean ± SD or as mean (99% confidence interval). $n = 21$.

HR = heart rate; MAP = mean arterial blood pressure; RAP = right atrial pressure; CI = cardiac index; SVRI = indexed systemic vascular resistance; PAP = mean pulmonary artery pressure; PVRI = indexed pulmonary vascular resistance; PAOP = pulmonary artery occlusion pressure; RVEDP = right ventricular end-diastolic pressure.

Statistically significant if $P < 0.01$ by paired t test or sign rank test.

Table 5**Hemodynamic Measurements in Children with Transplanted Hearts**

	Baseline	Dexmedetomidine	Change (99% confidence interval)	P
HR (bpm)	89 ± 18	79 ± 16	−9 (−14 to −5)	<0.0001
MAP (mm Hg)	60 ± 8	75 ± 18	15 (8 to 22)	<0.0001
RAP (mm Hg)	6 ± 3	8 ± 2	1.3 (0.4 to 2.1)	0.0003
CI (L/min/m ²)	3.2 ± 0.5	3.0 ± 0.8	0.2 (−0.4 to 0.1)	0.0929
SVRI (Wood u × m ²)	17.0 ± 3.2	23.0 ± 7.2	5.9 (2.9 to 8.9)	<0.0001
PAP (mm Hg)	17 ± 4	20 ± 4	3.0 (1.5 to 4.5)	0.0001
PVRI (Wood u × m ²)	2.7 ± 1.0	3.0 ± 1.0	0.3 (−0.2 to 0.7)	0.1238
PVRI/SVRI	0.17 ± 0.07	0.15 ± 0.08	−0.02 (−0.05 to 0.01)	0.0636
PAOP (mm Hg)	8 ± 2	11 ± 2	2.6 (1.7 to 3.5)	<0.0001
RVEDP (mm Hg)	7 ± 2	8 ± 2	0.5 (−0.2 to 3.0)	0.0216

Data are expressed as mean ± SD or as mean (99% confidence interval). $n = 21$.

HR = heart rate; MAP = mean arterial blood pressure; RAP = right atrial pressure; CI = cardiac index; SVRI = indexed systemic vascular resistance; PAP = mean pulmonary artery pressure; PVRI = indexed pulmonary vascular resistance; PAOP = pulmonary artery occlusion pressure; RVEDP = right ventricular end-diastolic pressure.

Statistically significant if $P < 0.01$ by paired t test or sign rank test.

Table 6

Hemodynamic Measurements by Dexmedetomidine Initial Loading Dose

	0.5 µg/kg			0.75 µg/kg			1 µg/kg		
	Baseline	Dexmedetomidine	P	Baseline	Dexmedetomidine	P	Baseline	Dexmedetomidine	P
HR (bpm)	83 ± 18	78 ± 17	0.0049	86 ± 16	76 ± 16	0.0007	93 ± 15	80 ± 17	0.0001
MAP (mm Hg)	58 ± 4	65 ± 11	0.0044	59 ± 9	76 ± 12	<0.0001	59 ± 8	80 ± 19	<0.0001
RAP (mm Hg)	6 ± 3	8 ± 2	0.0007	5 ± 2	7 ± 2	0.0016	7 ± 1	8 ± 2	0.0066
CI (L/min/m ²)	3.2 ± 0.5	3.0 ± 0.7	0.0447	3.1 ± 0.4	3.1 ± 0.8	0.8926	3.6 ± 0.6	3.6 ± 0.6	0.7905
SVRI (Wood u × m ²)	16.17 ± 2.86	19.89 ± 7.15	0.0102	17.22 ± 2.72	23.27 ± 6.26	0.0003	14.87 ± 2.98	20.58 ± 6.21	0.0004
PAP (mm Hg)	22 ± 10	25 ± 9	0.0276	20 ± 9	24 ± 10	0.0034	25 ± 10	27 ± 7	0.4247
PVRI (Wood u × m ²)	3.85 ± 1.64	4.16 ± 1.71	0.1953	3.97 ± 2.80	4.35 ± 2.57	1	4.55 ± 2.85	4.30 ± 1.81	0.3617
PVRI/SVRI	0.25 ± 0.11	0.23 ± 0.12	0.3269	0.25 ± 0.22	0.21 ± 0.17	0.424	0.31 ± 0.22	0.23 ± 0.12	0.023
PAOP (mm Hg)	8 ± 2	10 ± 3	0.0045	8 ± 3	10 ± 3	0.0106	8 ± 2	11 ± 2	0.0002
RVEDP (mm Hg)	6 ± 2	8 ± 1	0.0007	7 ± 3	8 ± 2	0.1603	8 ± 2	10 ± 2	0.0032

Data are expressed as mean ± SD. *n* = 14 in each group.

HR = heart rate; MAP = mean arterial blood pressure; RAP = right atrial pressure; CI = cardiac index; SVRI = indexed systemic vascular resistance; PAP = mean pulmonary artery pressure; PVRI = indexed pulmonary vascular resistance; PAOP = pulmonary artery occlusion pressure; RVEDP = right ventricular end-diastolic pressure.

Statistically significant if *P* < 0.01 by paired *t* test or sign rank test.