Adverse Effects of High-Dose vs Standard-Dose Dexmedetomidine in Cardiac Surgery Patients: A Retrospective Cohort Study

Leo Leung, BSc(Pharm); Erica Wang, BSc(Pharm), PharmD, ACPR, BCPS; Bobby Lee, MD, FRCSC

Background

- Dexmedetomidine is an α-2 agonist used for sedation in the critically-ill
- Reportedly, it has less respiratory depression, more hypotension, and more bradycardia compared to other sedatives
- The dexmedetomidine monograph recommends 0.2-0.7mcg/kg/hr as standard dosing, but higher doses have been used in the critically-ill
- In cardiac surgery patients, the safety of higher-than-recommended doses (i.e. 1.0-1.5mcg/kg/hr or higher) is not known

Objective

To determine whether there is an increased risk of adverse effects with higher-than-recommended doses of dexmedetomidine in cardiac surgery patients.

Methods

Design: Retrospective cohort study via health record review

Inclusion Criteria:

- Adult patients (≥18 years old)
- Admitted to St. Paul's Hospital (SPH) cardiac surgery intensive care unit (CSICU) after open heart surgery with coronary artery bypass grafting (CABG), valve surgery, or both between April 2013 to July 2017
- Received dexmedetomidine IV post-operatively for any indication

Exclusion Criteria:

- Patients who received heart transplant, left ventricular assist devices, laser lead extractions, or transcatheter valve procedures

Primary Outcome:

- Difference in the rate of hypotension[1] or bradycardia[2] in those on:
  High-dose dexmedetomidine (HiD) [>1mcg/kg/hour*] vs
  Standard-dose dexmedetomidine (StD) [≤1mcg/kg/hour*]

Secondary Outcomes:

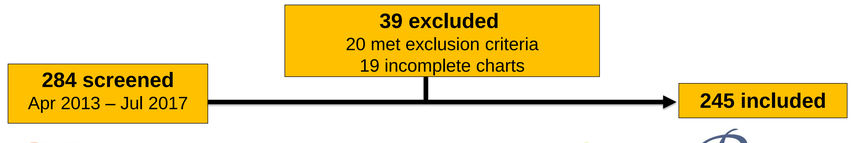
- Difference in the rates of: hypotension, bradycardia, hypoglycemia, arrhythmias between HiD and StD dexmedetomidine
- Difference in the rate of hypotension or bradycardia in those who received >0.7mcg/kg/hour vs ≤0.7mcg/kg/hour of dexmedetomidine

**at any point during the infusion, regardless of duration*
[1]hypotension: MAP <60mmHg or if vasopressors initiated
[2]bradycardia: heart rate <50bpm or if epicardial pacing required

Statistics:

- Descriptive statistics and multivariate analysis via logistic regression
- Sample size: need 63 patients per arm to achieve 80% power
  (α = 0.05, effect size = 20%, SD = 0.40)
- Statistical significance: p<0.05

Figure 1. Flow Diagram



Results

Table 1. Baseline and Surgical Characteristics

	HiD (n = 49)	StD (n = 196)
Mean Age, years ± SD	63.9 ± 10.9	65.2 ± 11.5
Males, n (%)	46 (93.6)	153 (78.1)
Past Medical History, n (%)		
Hypertension	37 (75.5)	149 (76.0)
HF	22 (44.9)	66 (33.7)
AF	12 (24.5)	43 (21.9)
VHD	12 (24.5)	40 (20.4)
Surgery Type, n (%)		
CABG	25 (51.0)	114 (58.8)
Valve Surgery	13 (26.5)	48 (24.7)
CABG & Valve Surgery	2 (4.1)	28 (14.4)
Mean CBP Time, min ± SD	119.6 ± 79.8	120.3 ± 76.6
Mean X-Clamp Time, min ± SD	88.1 ± 53.3	90.8 ± 2.3
Mean Intubation Time, hrs ± SD	20.5 ± 21.4	10.3 ± 16.3

Table 2. Dexmedetomidine Infusion Characteristics

	HiD (n = 49)	StD (n = 196)
Mean Infusion Duration, hrs ± SD	35.6 ± 26.0	12.8 ± 12.3
Concomitant Vasoactive Agents, n (%)	40 (81.6)	161 (82.1)
Norepinephrine	27 (55.1)	120 (61.2)
Epinephrine	11 (22.4)	29 (14.8)
Milrinone	15 (30.6)	47 (24.1)
Other	9 (18.3)	43 (21.9)
Concomitant Sedatives, n (%)	18 (32.7)	52 (24.5)
Propofol	11 (22.4)	44 (22.4)
Opioid infusion	6 (12.2)	6 (3.1)
Other	1 (2.0)	2 (1.0)

Table 3. Mean Change in Hemodynamics following Dexmedetomidine

	Baseline		Post-Infusion of Dexmedetomidine			
	MAP (mmHg±SD)	HR (bpm±SD)	MAP (mmHg±SD) Min	MAP (mmHg±SD) Max	HR (bpm±SD) Min	HR (bpm±SD) Max
HiD	74 ± 12	87 ± 19	56 ± 7	96 ± 16	64 ± 13	102 ± 22
StD	74 ± 12	85 ± 15	57 ± 7	90 ± 14	70 ±11	95 ± 18

Figure 2. Dose of Dexmedetomidine Used (mcg/kg/hr)

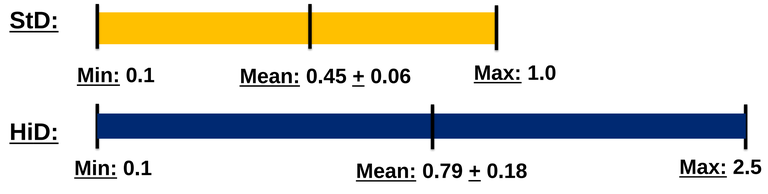
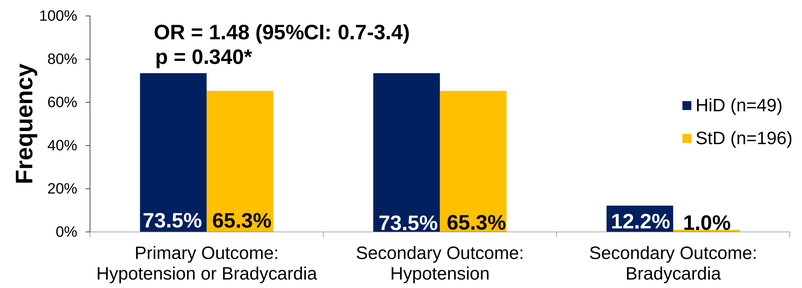
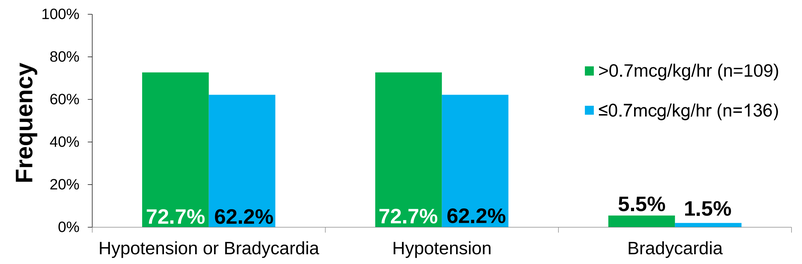


Figure 3. Primary Outcome: Rate of Hypotension or Bradycardia in those on HiD vs StD dexmedetomidine (n = 245)



**Adjusted for: age, sex, PMHx, surgery type, concomitant sedatives and vasoactive agents*

Figure 4. Rate of Hypotension or Bradycardia in those on dexmedetomidine >0.7 vs ≤ 0.7 mcg/kg/hr (n = 245)



Other Results

- All bradycardic episodes were transient and lasted < 1 hour
- Despite hypotension, vasopressor initiation or up-titration rates were similar in HiD vs StD: 11 (30.6%) vs 39 (30.5%)
- Other results for HiD vs StD: Arrhythmias: 14 (28.9%) vs 45 (23.4%)
  Hyperglycemia: 7 (14.6%) vs 29 (15.0%)

Discussion

- First study of high-dose dexmedetomidine after cardiac surgery and the largest study of high-dose vs standard-dose in the critically-ill
- Rate of primary outcome is high, but majority of patients did not require vasopressor initiation or dose escalation
- Considerable overlap of dosing exists between HiD vs StD groups
- Compared to monograph and previous studies in critically-ill patients, this study showed higher rate of hypotension and lower rate of bradycardia
- Limitations include: retrospective study, power not achieved, generalizability of outcome

Conclusions

- In critically-ill patients after cardiac surgery, the rate of hypotension or bradycardia is higher with high-dose dexmedetomidine compared to standard-dose, but was not statistically significant
- Larger studies with adequate statistical power may be warranted to fully elicit adverse effects of high-dose dexmedetomidine in the cardiac surgery population

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