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A pilot analysis of the association between types of conscious sedation drugs and outcomes in transfemoral aortic valve replacement performed without general anesthesia

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Abstract

Objective—The types of agents used for monitored anesthesia care (MAC) and their possible differential effects on outcomes have received less study despite increased use over general anesthesia (GA) in transfemoral aortic valve replacements (TAVRs). In this pilot analysis of patients undergoing TAVR using MAC, we described the anesthetic agents used and sought to investigate the possible association of anesthetic agent choice with outcomes, and the extent to which total weight and time-adjusted doses of anesthetics declined with increasing 10-year age-increments.

Design—Retrospective observational study.

Setting—Tertiary teaching hospital.

Participants—93 participants scheduled to undergo TAVR with a primary plan of conscious sedation between November 2014 and June 2016 were included.

Intervention—None.

Measurements and Main Results—Types of MAC were divided into four primary groups, but we focused on two groups: propofol (n=39) and dexmedetomidine plus propofol (n=34). Conversion to GA occurred in 6 participants (6.45%) and was not associated with type of sedation received. We also compared patients receiving dexmedetomidine to those who did not in accordance with our a priori analytic plan. There were no associations between the use of dexmedetomidine and postoperative delirium or ICU/hospital length of stay. There were also no significant trends in medication dose adjustments seen across increasing 10-year age increments.

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Conclusions—A wide breadth of MAC medications is in use among TAVR patients and does not support differences in outcomes. Despite recommendations to reduce anesthetic drug dosing in the elderly, no significant trends in dose reduction with increasing age were noted.

Keywords

TAVR; monitored anesthesia care; dexmedetomidine; age-adjusted dosing; elderly

Introduction

Transfemoral aortic valve replacement (TAVR) involves replacing a malfunctioning aortic valve via a catheter-deployed prosthetic valve. Although first performed in 2001, TAVR received approval by the Food and Drug Administration in 2011. TAVR was originally only performed in high-risk surgical patients;¹ however, with new valve technology and physician experience, TAVR is now an acceptable alternative for some patients at intermediate risk for conventional valve surgery.^{2, 3}

The choice of general anesthesia (GA) versus monitored anesthesia care (MAC) in TAVR has received significant attention in recent years.^{2,4,5} While both GA and MAC provide safe options for TAVR anesthesia, some studies have suggested that MAC is associated with significantly shorter procedure time, ICU length of stay, hospital length of stay, and lower costs as compared to GA.^{6–8} These findings have not been universal, as pooled data from 7 observational studies with a total of 1542 patients demonstrated no significant difference in 30-day mortality, cardiac-/procedure-related mortality, stroke, MI, sepsis, acute kidney injury, procedure time, and duration of hospital stay.^{2, 9, 10} Nevertheless, there has been a clear shift toward MAC for many TAVR patients, but very few publications have detailed the amounts and types of drugs used for sedation or any possible associations with outcomes among the different drugs used for MAC.

Accordingly, in the present pilot study, we sought to analyze the different ways of conducting MAC for TAVR at our institution, the association of choice of anesthetic used with outcomes, and the extent to which total doses of MAC anesthetics declined with increasing 10-year age-increments.^{11–13}

Methods

The study protocol received local Institutional Review Board approval and was registered and conducted in accordance with the protocol as described on ClinicalTrials.gov (NCT02786264). Subsequent edits to the plan of analysis were performed as part of the peer review process.

Study Population

This retrospective observational study included all patients who underwent TAVR with a primary plan for MAC administered by an anesthesiologist from November 1, 2014 to June 22, 2016 at the authors' institution. In total, 93 patients had a plan for MAC as their primary anesthetic technique for TAVR during this period.

Data Sources

For cohort identification, we queried our local institutional Multicenter Perioperative Outcomes Group database for procedures using the CPT codes 33361 or 33362, and then a detailed chart review was undertaken for this population.

Patient demographic data included age, sex, ethnicity, and race. Preoperative variables included height, weight, ASA physical status score, NYHA CHF classification, left ventricular ejection fraction (LVEF), body mass index (BMI - calculated as the weight in kilograms divided by the height in meters squared). Dichotomous variables were created for the preoperative presence of a comorbid diagnosis for each of the following conditions: alcoholism, anxiety disorder, atrial fibrillation, cerebrovascular disease, congestive heart failure, coronary artery disease, diabetes, hypertension, depression, obstructive sleep apnea (OSA), peripheral vascular disease, psychosis, renal disease, and substance abuse. Postoperative outcomes included procedure length, chart-obtained presence of post-procedure delirium, conversion to GA, ICU length of stay, and hospital length of stay. Depth of sedation was not recorded consistently in the anesthesia record.

Statistical Analysis

The continuous variables were summarized by median (IQR), and were compared by group using the Wilcoxon rank sum test. The categorical variables were represented as n (%) and compared by group using the Fisher's exact test. The preoperative variables (demographics, perioperative predictor variables) were compared to understand whether there was a significant difference in the characteristics of the patients receiving different monitored anesthesia care anesthetic regimens. The Jonckheere-Terpstra trend test was used to compare the age-adjusted dosing for the different anesthetics. All the statistical analyses were performed using SAS v9.4 (Cary, NC) and a two-sided p-value of less than 0.05 was considered to be statistically significant.

Results

Descriptive Aim: Types of Monitored Anesthesia Care

After an initial survey of anesthetics used in TAVRs, we grouped different MAC techniques into four broad categories defined as follows. A "propofol dominant" type (N=39; 42%) was defined as any MAC that included propofol infusions or injections in the absence of dexmedetomidine. These patients may have also received injections of fentanyl, remifentanyl, or midazolam. A "dexmedetomidine dominant" type (N=16; 17%) was defined as any MAC anesthetic that included dexmedetomidine infusions in the absence of propofol. These patients may have also received injections of fentanyl, remifentanyl, or midazolam. A "dexmedetomidine plus propofol" type (N=34; 37%) was similarly defined as any MAC that included both propofol and dexmedetomidine and may have included fentanyl, remifentanyl, or midazolam. A final "fentanyl dominant" type (N=4; 4%) consisted of any MAC that included neither propofol nor dexmedetomidine and consisted of intermittent fentanyl boluses with or without midazolam. As the "dexmedetomidine dominant" and "fentanyl dominant" groups had limited sample size, we decided to focus on the "propofol dominant" and "dexmedetomidine plus propofol" groups for analysis of outcomes.

Table 1 shows a descriptive analysis of preoperative demographic and comorbid variables by type of MAC used. No statistically significant differences among the two groups were found.

Association of type of monitored anesthesia care with conversion to GA

A total of six cases (6.45%) were identified as requiring conversion to GA. There was no significant association between type of MAC and conversion to GA (see Table 2).

Association of outcomes between those receiving dexmedetomidine versus those without

In accordance with our a priori analytic plan, we examined whether delirium, ICU length of stay, or hospital length of stay were different between those who received dexmedetomidine and those who did not. None of these variables were significantly associated with the receipt of dexmedetomidine (see Table 3). In addition, none of the variables were significantly different when compared among the two major MAC groups (see Table 2).

Age-adjusted dosing

In accordance with our a priori plan, we looked at the age-adjusted dosing for the different anesthetics described above. To obtain a consistent dose across procedures of varying length, we calculated the dose parameter as total dose of each anesthetic divided by the patients' weights and procedure lengths. There was no significant trend observed by decade of age for midazolam ($p = 0.6315$), fentanyl ($p = 0.7943$), propofol ($p = 0.7366$), or dexmedetomidine ($p = 0.6252$) dosing (Figure 1).

Discussion

As expected from our a priori hypothesis, the four main anesthetics used for MAC were propofol, dexmedetomidine, fentanyl analogues, and midazolam. Looking at the conversions of MAC cases to GA, we saw a conversion rate of 6.45% – much lower than other studies, which had conversion rates of up to 17%.¹⁴ This lower-than-expected rate of conversions limited the anticipated power of the present analysis. Nevertheless, it is worthwhile to look at the details of the conversions that took place. In our study, two of the six conversions may have been associated with respiratory depression. Hypercapnia was experienced by both patients, suggesting the possibility that drug-induced depression of the ventilatory response to CO₂ by drugs other than dexmedetomidine may have played a role.¹⁵ Of the remaining four conversions, two were due to procedural issues and two had no clearly identifiable causal factor based on chart review.

Although our study did not demonstrate a significant difference in any of the prespecified outcomes, these findings should be considered only as pilot preliminary data due to the small sample size. Larger studies may provide more definitive answers to questions regarding the association of MAC anesthetic type and important patient outcomes.

Regarding appropriate adjustment of anesthetics for age, it is well accepted that anesthetic doses should be reduced in the elderly; however, we saw no evidence that total doses of anesthetics were reduced with increasing decade of age. This was partially due to certain age

groups having limited number of patients. This finding is consistent with the notion that providers may not age-adjust anesthetic dosing in the extreme elderly as our group has shown previously.^{12, 16} However, we hasten to add that the rarity of poor outcomes in the present study did not allow for an assessment of whether further adjustments in MAC anesthetic dosing in the extreme elderly population would lead to improvements in care.^{17, 18}

Limitations

This study had several limitations. Being a retrospective observational study, we were performance limited by the accuracy and completeness of the data recorded in the chart. Furthermore, as mentioned above, our findings were limited by the paucity of negative outcomes that were seen. For example, it was of interest to us to explore whether dexmedetomidine was associated with lower rates of delirium as has been previously seen. However, in our own study, only three patients experienced delirium.¹⁹ Although there was no significant difference in the presence of delirium between the groups with dexmedetomidine and those without, further studies with much larger sample sizes would be needed to explore this possibility in the TAVR population. It is also important to note that for our analysis of age-adjusted anesthetic dosing, patients who received a combination of the four drugs were treated as separate data points for each drug. Our analysis does not reflect the effect on dosing that might result from the combination of the different drugs and their possible synergies.

In conclusion, the present study demonstrated significant variability in the choice of anesthetics used for MAC of TAVR patients at our institution. Overall rates of conversion to general anesthesia were below prior published reports, and no difference in perioperative or postoperative outcomes were detected in association with the anesthetic agents that were used for CS. Last, anesthetic dosing was minimally adjusted for age, and the question of what such appropriate adjustments should be remains an area in need of further dedicated study.

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Figure 1.
Weight and procedure length-adjusted dosing by age group.

Table 1

Summary statistics of demographics among the different types of monitored anesthesia care.

	MAC Groups			
	Propofol and Dexmedetomidine (N=34)	Propofol drip only (N=39)	Total (N=73)	p-value
Age (years)				
Median (IQR)	84.0 (78.0–88.0)	87.0 (81.0 – 90.0)	87.0 (80.0 – 89.0)	0.17
Sex				
Female	20 (58.82%)	15 (38.46%)	35 (47.95%)	0.08
Male	14 (41.18%)	24 (61.54%)	38 (52.05%)	
Race/Ethnicity				
White or Caucasian	31 (91.18%)	34 (87.18%)	65 (89.04%)	0.75
Black	1 (2.94%)	1 (2.56%)	2 (2.74%)	
Hispanic or Latino	1 (2.94%)	2 (5.13%)	3 (4.11%)	
Other	1 (2.94%)	0 (0.00%)	1 (1.37%)	
Unknown	0 (0.00%)	2 (5.13%)	2 (2.74%)	
Height (m)				
Median (IQR)	1.6 (1.6–1.7)	1.6 (1.6 – 1.7)	1.6 (1.6 – 1.7)	0.92
Weight (kg)				
Median (IQR)	71.5 (59.1 – 80.5)	76.6 (65.6 – 85.1)	73.7 (62.0 – 83.2)	0.17
BMI				
Median (IQR)	25.6 (22.1 – 29.3)	29.2 (23.9 – 32.3)	26.7 (23.9 – 30.7)	0.13
ASA Physical Status Score (1–6)				
3	5 (14.71%)	3 (7.69%)	8 (10.96%)	0.46
4	29 (85.29%)	36 (92.31%)	65 (89.04%)	
NYHA CHF Classification (1–4)				
2	5 (14.71%)	1 (2.56%)	6 (8.22%)	0.19
3	24 (70.59%)	32 (82.05%)	56 (76.71%)	
4	5 (14.71%)	6 (15.38%)	11 (15.07%)	
Left Ventricular Ejection Fraction				
Median (IQR)	63.0 (59.0 – 67.0)	62.0 (55.0 – 66.0)	62.0 (55.0 – 66.0)	0.51
Alcoholism				
No	34 (100.00%)	38 (97.44%)	72 (98.63%)	1.00
Yes	0 (0.00%)	1 (2.56%)	1 (1.37%)	
Anxiety Disorder				
No	30 (88.24%)	35 (89.74%)	65 (89.04%)	1.00
Yes	4 (11.76%)	4 (10.26%)	8 (10.96%)	
Atrial Fibrillation				
No	22 (64.71%)	18 (46.15%)	40 (54.79%)	0.11
Yes	12 (35.29%)	21 (53.85%)	33 (45.21%)	

	MAC Groups			
	Propofol and Dexmedetomidine (N=34)	Propofol drip only (N=39)	Total (N=73)	p-value
Cerebrovascular Disease				
No	29 (85.29%)	38 (97.44%)	67 (91.78%)	0.09
Yes	5 (14.71%)	1 (2.56%)	6 (8.22%)	
CHF				
No	15 (44.12%)	17 (43.59%)	32 (43.84%)	0.96
Yes	19 (55.88%)	22 (56.41%)	41 (56.16%)	
CAD				
No	12 (35.29%)	13 (33.33%)	25 (34.25%)	0.86
Yes	22 (64.71%)	26 (66.67%)	48 (65.75%)	
Diabetes				
No	24 (70.59%)	27 (69.23%)	51 (69.86%)	0.90
Yes	10 (29.41%)	12 (30.77%)	22 (30.14%)	
Hypertension				
No	4 (11.76%)	5 (12.82%)	9 (12.33%)	1.00
Yes	30 (88.24%)	34 (87.18%)	64 (87.67%)	
Depression				
No	30 (88.24%)	35 (89.74%)	65 (89.04%)	1.00
Yes	4 (11.76%)	4 (10.26%)	8 (10.96%)	
Obstructive Sleep Apnea				
No	32 (94.12%)	33 (84.62%)	65 (89.04%)	0.27
Yes	2 (5.88%)	6 (15.38%)	8 (10.96%)	
Peripheral Vascular Disease				
No	27 (79.41%)	35 (89.74%)	62 (84.93%)	0.22
Yes	7 (20.59%)	4 (10.26%)	11 (15.07%)	
Psychosis				
No	34 (100.00%)	39 (100.00%)	73 (100.00%)	--
Yes	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Renal Disease				
No	22 (64.71%)	30 (76.92%)	52 (71.23%)	0.25
Yes	12 (35.29%)	9 (23.08%)	21 (28.77%)	
Substance Abuse				
No	34 (100.00%)	39 (100.00%)	73 (100.00%)	--
Yes	0 (0.00%)	0 (0.00%)	0 (0.00%)	

Table 2

Descriptive statistics of perioperative and postoperative outcomes for the different types of monitored anesthesia care.

	MAC Groups			
	Propofol and Dexmedetomidine (N=34)	Propofol drip only (N=39)	Total (N=73)	p-value
Conversion to GA				
No	31 (91.18%)	38 (97.44%)	69 (94.52%)	0.33
Yes	3 (8.82%)	1 (2.56%)	4 (5.48%)	
Delirium				
No	34 (100.00%)	38 (97.44%)	72 (98.63%)	1.00
Yes	0 (0.00%)	1 (2.56%)	1 (1.37%)	
Procedure Length (min)				
Median (IQR)	114.5 (102.0 – 137.0)	100.0 (87.0 – 123.0)	107.0 (91.0 – 126.0)	0.06
Hospital Stay Length (days)				
Median (IQR)	2.0 (2.0 – 3.0)	2.0 (2.0 – 3.0)	2.0 (2.0 – 3.0)	0.71
ICU Stay Length (days)				
Median (IQR)	1.0 (1.0 – 1.0)	1.0 (1.0 – 2.0)	1.0 (1.0 – 1.0)	0.45

Table 3

Summary statistics and comparison of postoperative outcomes between the dexmedetomidine and the other group

	Dexmedetomidine (N = 50)	Other (N = 43)	p-value
Delirium			
No	49 (98.00%)	41 (95.35%)	0.59
Yes	1 (2.00%)	2 (4.65%)	
Hospital Stay Length (days)			
Median (IQR)	2.0 (2.0 – 3.0)	2.0 (2.0 – 3.0)	0.81
ICU Stay Length (days)			
Median (IQR)	1.0 (1.0 – 1.0)	1.0 (1.0 – 2.0)	0.26