

The Effect of Dexmedetomidine on Perioperative Hemodynamics in Patients Undergoing Craniotomy

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BACKGROUND: The perioperative course of patients undergoing intracranial surgery is frequently complicated by hypertensive episodes. Dexmedetomidine (DEX), an α -2 adrenoreceptor agonist, is gaining popularity in neuroanesthesia, because its sympatholytic and antinociceptive properties may improve hemodynamic stability at critical moments of surgery. We designed this study to assess the efficacy of DEX in controlling hypertensive responses in patients undergoing intracranial surgery. **METHODS:** Patients scheduled for elective craniotomy were randomly assigned to receive either sevoflurane–opioid or sevoflurane–opioid–DEX anesthesia. Bispectral index was used to maintain a similar level of hypnosis in both groups (40–50). Opioids, sevoflurane, and vasoactive medications were titrated in a routine manner, at the discretion of the blinded anesthesiologist managing the case, to maintain systolic blood pressure (SBP) targeted within 90–130 mm Hg and heart rate (HR) between 50 and 90 bpm. Hemodynamic variables were continuously recorded and stored on a computer for analysis. Efficacy of the anesthetic technique in controlling SBP or HR is inversely proportional to the area under the curve (AUC) outside the targeted range. Areas under the curves above and below targeted ranges for SBP-time (AUCsbp mm Hg * min/h) and HR-time (bpm * min/h) were compared. Coefficient of variation was used to assess hemodynamic stability. **RESULTS:** Seventy-two patients were recruited for the study. Computerized records of 56 patients only were analyzed because of technical problems with data collection in 14 cases. AUCsbp for above the targeted range was significantly lower for patients in the DEX group ($P = 0.044$). The coefficient of variation for SBP or HR did not differ between groups. A significantly smaller proportion of patients in the DEX group required treatment with antihypertensive medications (12 of 28, 42% vs 24 of 28, 86%, $P = 0.0008$). The DEX group required fewer opioids in the intraoperative period, but there were no differences in the use of sevoflurane. In the postanesthesia care unit, patients in the DEX group had fewer hypertensive episodes (1.25 ± 1.55 vs 2.50 ± 2.00 , $P = 0.0114$) and were discharged earlier (91 ± 17 vs 130 ± 27 min, $P < 0.0001$). There were no differences in the requirement for postoperative opioids or antiemetics. **CONCLUSIONS:** By using indices, which assess a global hemodynamic stability of the anesthetic, we determined that intraoperative DEX infusion was effective for blunting the increases in SBP perioperatively. The use of DEX did not increase the incidence of hypotension or bradycardia, common side effects of the drug.

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Periodic hypertension in neurosurgical patients is associated with intracranial hemorrhage and

prolonged hospital stay.¹ Even given current neuroanesthesia management, hemodynamic stability may be challenging, especially in hypertensive patients. An anesthetic technique that improves perioperative hemodynamics without increasing the incidence of undesirable events (such as increased intracranial pressure, prolonged recovery, etc.) is desirable.

Dexmedetomidine (DEX), an α -2 agonist with sedative, sympatholytic, and analgesic properties, could be a potentially useful anesthetic adjuvant for neurosurgical cases.² Two investigations have examined its use in patients undergoing intracranial surgery.^{3,4} Both studies concluded that the addition of DEX improves perioperative hemodynamic control. In these trials, the authors controlled arterial blood pressure with a prescribed incremental dosing of anesthetics. No patient in either study required antihypertensive medications.

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It is difficult to translate the results of these trials to clinical practice. Experienced anesthesiologists often attempt to anticipate and blunt the hypertensive responses seen in varying degrees at critical moments of surgical stimulation (e.g., pinning, incision). Additionally, it may take a long time to treat acute intraoperative hypertension using anesthetics, and there may be a subsequent period of hypotension due to overcompensation. Most practicing anesthesiologists rely on antihypertensive drugs for the rapid control of elevated arterial blood pressure, especially during emergence, when volatile anesthetics and narcotics need to be discontinued for rapid awakening. Relatively high doses of antihypertensive drugs, such as labetalol, nicardipine, or esmolol, are commonly used in neurosurgery, regardless of the anesthetic technique.^{5,6}

We therefore designed a study to determine whether the addition of DEX would provide a greater perioperative hemodynamic stability in patients undergoing intracranial procedures. One of the main goals was to use a typical neuroanesthetic regimen as well as common methods to control arterial blood pressure. Patients in both study arms were treated with adjustments in the concentration of volatile anesthetic or opioid use, or were administered antihypertensive drugs on an as-needed basis at the discretion of the blinded anesthesiologist. A coefficient of variation (CV) was used to compare variability (instability) of systolic blood pressure (SBP) and heart rate (HR). A global hemodynamic control was assessed by computing area under the curve (AUC) either above or below predetermined limits (e.g., beyond the clinical goals for SBP and HR ranges).

METHODS

Patient Selection

The study protocol was approved by the IRBA of the New York University and Rush University Medical Centers, and all subjects provided informed consent. Patients, 18–65 yr, scheduled for elective resection of a brain tumor, intracranial vascular lesion, or epileptic focus were approached. Consenting patients were randomized to one of two anesthetic groups: sevoflurane–opioid–DEX or sevoflurane–opioid–placebo (PLB). Excluded from the study were patients with significant laboratory abnormalities, patients with advanced heart block, or known allergic reaction to any of the study medications. The anesthetic was managed by experienced neuroanesthesiologists blinded to DEX or placebo regimen.

Anesthetic Management

Standard intraoperative and bispectral index (BIS) monitoring were used. The patients received 5 mL/kg of normal saline IV before induction. After administration of oxygen by mask, general anesthesia was induced with lidocaine (1 mg/kg), propofol (up to 2 mg/kg), and fentanyl (up to 3 μ g/kg IV). Tracheal

intubation was facilitated with vecuronium (0.1 mg/kg). Invasive arterial monitoring was established after induction. Patients were moderately hyperventilated during the case (PACO₂ 28–32 mm Hg). The infusion of a study drug or placebo was initiated after intubation to avoid concomitant hypertension associated with the initial loading dose of DEX. Patients in the DEX group received an initial loading dose of 1 μ g/kg of DEX over 10 min, followed by a continuous infusion of 0.5 μ g \cdot kg⁻¹ \cdot h⁻¹. Patients in the PLB group received an equivalent volume of normal saline. Anesthesia was maintained with sevoflurane in air/oxygen mixture (60%/40%) and remifentanyl (0.05–0.2 μ g \cdot kg⁻¹ \cdot min⁻¹). A study drug loading was completed before Mayfield or Sugita pins application (pinning). Fentanyl boluses were administered before pinning and skin incision (2–5 mg/kg). The anesthesiologist was allowed to administer additional doses of fentanyl at his/her discretion. A concentration of sevoflurane was titrated to maintain a BIS of 50 until closing of the dura. Sevoflurane concentration was reduced to maintain a BIS of 60–70 thereafter and discontinued during skin closure. DEX or placebo infusions were stopped at approximately 20 min before the end of the procedure. All patients received ondansetron 4 mg and underwent routine reversal of neuromuscular blockade. Patients were awakened and extubated in the operating room (OR) and were transferred to the postanesthesia care unit (PACU) after following simple commands. Anesthesiologist and nurses who were unaware of anesthetic technique managed postoperative recovery of the study patients.

Hemodynamic Management

Hemodynamic events that required treatment were defined as (1) hypotension: SBP <90 mm Hg, (2) hypertension: SBP >130 mm Hg, (3) bradycardia: HR <50 bpm, and (4) tachycardia: HR >90 bpm. The anesthesiologist was permitted to treat hemodynamic events at any time by adjusting the sevoflurane concentration, changing the remifentanyl infusion rate, administering boluses of fentanyl and incremental doses of ephedrine 5 mg, phenylephrine 100 μ g, labetalol 10 mg, hydralazine 5 mg, or metoprolol 2 mg IV. In addition, the anesthesiologist was allowed to administer analgesics and/or antihypertensive drugs in anticipation of painful (hemodynamically stimulating) stimuli, which is consistent with the usual practice. Hemodynamic management goals in the PACU were similar to the approach used in the OR. PACU personnel administered analgesics, antiemetics, and vasoactive drugs as needed (without consultation with the research staff).

Data Collection

The intraoperative hemodynamic data obtained from the Phillips IntelVue monitor and Drager 6000 anesthesia machine were acquired at a frequency of 30 samples per minute using the analog-digital data

Table 1. Demographic Data

	Placebo (n = 28)		Dexmedetomidine (n = 28)		P
	Mean	SD	Mean	SD	
Age	47.7	13.3	44.3	17.8	0.4230
Weight (kg)	72.3	12.8	73.4	13.9	0.7578
Sex					0.3972
Female	8	29%	11	39%	
Male	20	71%	17	61%	
	No.	Percentage	No.	Percentage	
ASA classification					0.4826
ASA 2	14	50	17	61	
ASA 3	13	46	11	39	
ASA 4	1	4	0	0	
Craniotomy for:					0.3383
Tumor resection	13	46	8	29	
Epilepsy	13	46	16	57	
Vascular lesion	2	7	4	14	
History of hypertension	7	25	7	25	1.000
Preoperative medication					
Any antihypertensive	7	25	6	21	0.7516
Beta-blockers	3	11	3	11	1.0000
Calcium channel blockers	0	0	1	4	0.3130
ACE-inhibitors	4	14	2	7	0.3875
	Mean	SD	Mean	SD	
Preinduction					
Blood pressure					
Systolic BP	129.5	19.8	126.4	21.3	0.5744
Diastolic BP	76.7	12.2	75.2	10.8	0.6211
Heart rate	79.4	5.3	83.4	5.4	0.0347*

sd = standard deviation; n = sample size; ACE = angiotensin converting enzyme.

* Statistically Significant at $\alpha = 0.05$.

acquisition system MetaVision (iMDSOFT, Needham, MA). All continuous signals (e.g., SBP, HR, BIS, and sevoflurane concentration) were processed through a 1-min median filter to remove artifacts. The technique of median filtering is widely used in various biomedical applications (including computerized processing of arterial blood pressure in the critical care setting) and is described elsewhere.^{7,8} Median filtering is a nonlinear signal enhancement technique for the smoothing of signals, the suppression of impulse noise and preserving of edges. In our case (one-dimensional), it consists of sliding a window of 30 samples along the signal, replacing the center sample by the median of the samples in the window. It measures central tendency over a time interval without being unduly affected by the extreme (and correspondingly implausible) spikes. Data before and after application of the filter were assessed visually (signal over time plot) to verify a proper artifact rejection without a loss of signal or trend information.

PACU data were collected from the patients' records. Although arterial blood pressure was monitored continuously, it was documented in 15 min intervals on the PACU record. We assessed hemodynamic stability by comparing the number of times a recorded SBP was above 130 mm Hg or below 90 mm

Hg. We also compared PACU use of analgesics, vasoactive drugs, antiemetics, and duration of the PACU stay.

Data and Statistical Analysis

A Microsoft SQL database was used to store and manipulate the data. Files with large segments of incongruous or incompletely acquired signal data were not included in the group comparative analysis.

We assessed global hemodynamic stability using the CV of SBP and HR. The CV is the ratio of the standard deviation of the mean to the mean, a statistic for comparing the degree of variation from one set of data to another, even if the means are different from each other. The total, positive (above the mean) and negative (below the mean) CVs were calculated. AUCs above 130 mm Hg and below 90 mm Hg were used to analyze the overall efficacy of an anesthetic in maintaining SBP and HR close to the targeted range. A detailed description of the methods can be found elsewhere.^{9,10}

Our data from the preliminary study¹¹ showed that CV for SBP in patients not treated with DEX is $13.3\% \pm 3\%$. A 20% reduction in the CVsbp was considered clinically relevant and feasible. We calculated that 56

Table 2. Areas Under the Curves and Coefficients for Variation for Systolic Blood Pressure and Heart Rate

	Placebo (n = 28)		Dexmedetomidine (n = 28)		P*
	Median	IQR	Median	IQR	
AUC _{SBP} (mm Hg * min/h)					
Total	86	42–162	76	52–166	0.9347
Above (130 mm Hg)	35	10–101	9	1–49	0.0444†
Below (90 mm Hg)	27	8–58	48	10–96	0.1609
AUC _{HR} (beats * min/h)					
Total	19	4–80	15	3–43	0.4959
Above (90 bpm)	12	0–59	8	0–26	0.6054
Below (50 bpm)	0	0–2	0	0–4	0.6659
	Mean	SD	Mean	SD	P*
CV _{SBP} (%)					
Total	12.6	2.8	12.1	3.2	0.5328
Positive	9.7	2.4	9.1	3.2	0.4048
Negative	6.2	3.0	6.4	2.4	0.7766
CV _{HR} (%)					
Total	10.3	3.5	11.5	4.8	0.2836
Positive	6.9	2.9	8.8	4.7	0.0780
Negative	6.5	3.4	6.6	2.9	0.8867
Intraoperative average					
SBP (mmHg)	106.5	9.9	102.2	9.4	0.0986
HR (bpm)	74.6	13.0	67.9	1.7	0.0277†

IQR = interquartile range (25th to 75th percentile); SD = standard deviation; SBP = systolic blood pressure; HR = heart rate; CV = coefficient of variation; bpm = beat per minute.

* P-value based on Student's t-test.

† Statistically significant at $\alpha = 0.05$.

patients would provide 90% power at $\alpha = 0.05$ to detect this difference. Seventy-two patients were enrolled in our studies to compensate for the possible dropouts. We used a two-tailed test for the primary outcome measure.

Normally distributed variables, such as patients' demographics, were analyzed using two-sided Student's *t*-test. χ^2 and Fisher's exact tests were used for intergroup comparison of ordinal variables. The non-parametric Wilcoxon–Mann–Whitney test was used for variables that were not normally distributed (including AUCs). Bonferroni's step-down method was used to correct for the multiple comparisons. Data are expressed as mean \pm SD for continuous normally distributed variables, as median and interquartile range for continuous non-normally distributed data, and as proportions or counts for categorical data. All tests were two-sided with an $\alpha = 0.05$ (a criterion for significance).

RESULTS

Seventy-two patients were recruited for the study. Two patients initially enrolled were subsequently removed from data analysis. One patient, randomized to the DEX group, had the study drug discontinued intraoperatively due to protracted surgery with a major blood loss with subsequent need for emergent angiography and phenobarbital therapy. The second patient (PLB group) was transported to the PACU tracheally intubated. All other patients were extubated

and responded to simple commands in the OR at the end of the operation.

The two groups were comparable regarding age, sex, weight, ASA physical status, history of arterial hypertension, and type of surgery (Table 1). Although preinduction HR was higher in DEX patients, the difference was not clinically significant. Technical problems posed limitations to complete file recovery of continuous signal data from the computerized records of 14 studied patients. These patients' data were excluded from analysis.

AUCsbp above the target 130 mm Hg was significantly smaller for patients in the DEX group (Table 2). This parameter is inversely related to the efficacy of the arterial blood pressure control in the critical high region. HR was within the targeted range for all patients, although it was slower for patients treated with DEX (67.9 vs 74.6 bpm, $P = 0.0277$). We did not find a difference between groups in other variables that assess overall hemodynamic stability.

The average end-tidal sevoflurane concentrations and BIS values were similar in both groups (Table 3). The mean remifentanyl infusion rate was lower in the DEX group ($0.08 \pm 0.04 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ vs $0.11 \pm 0.05 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, $P = 0.0182$). Significantly fewer patients in the DEX group required pharmacologic intervention to control SBP intraoperatively (12 of 28, 43% vs 24 of 28, 86%). Somewhat surprisingly, more patients in the PLB group required treatment with ephedrine (11 of 28, 39% vs 3 of 28, 11%, $P =$

Table 3. Intraoperative Management

	Placebo (n = 28)		Dexmedetomidine (n = 28)		P
	Mean	SD	Mean	SD	
Sevoflurane					
Mean (% ET)	1.156	0.378	1.001	0.368	0.2185
CV	40.52	40.11	35.64	11.15	0.6240
Fentanyl*					
Induction (µg/kg)	2.27	0.71	1.93	0.70	0.1486
Rest of case (µg/kg)	2.6	1.9	1.9	1.0	0.1486
Remifentanyl (µg/kg)	27	13	19	11	0.0229†
Remifentanyl (µg/kg/min)	0.112	0.056	0.080	0.039	0.0182†
BIS					
Mean	48.3	5.3	46.3	6.4	0.3345
CV	16.3	6.5	16.3	5.7	0.9923
Time periods					
Surgical duration (h)	4.4	1.7	4.3	2.1	0.9360
Dressing-extubation (min)	10.4	8.5	11.4	7.0	0.6213
Dressing-simple response (min)	18.0	9.5	23.0	12.2	0.1123
Fluids					
EBL (mL/kg/h)	0.54	0.39	0.96	1.74	0.2237
IV Fluids (mL/kg/h)	7.6	4.7	7.3	6.1	0.7944
Urine output (mL/kg/h)	2.2	1.4	2.2	2.7	0.9698
	Count (%)	Median (IQR)	Count (%)	Median (IQR)	
BP Meds*					
Any	24 (86)		12 (43)		0.0008†
Labetalol	22 (79)	22.5 (15–50) mg	11 (39)	25 (15–40) mg	0.0084†
Metoprolol	1 (4)	5 mg	3 (11)	5 (5–10) mg	0.2994
Hydralazine	14 (50)	10 (10–20) mg	4 (14)	12.5 (10–17.5) mg	0.0084†
Any	14 (50)		6 (21)		0.0257†
Phenylephrine	6 (21)	150 (100–400) µg	4 (14)	175 (95–450) µg	0.4853
Ephedrine	11 (39)	10 (5–25) mg	3 (11)	10 (5–10) mg	0.0271†

SD = standard deviation; IQR = interquartile range (25th percentile to 75th percentile); BP = blood pressure; ET = end-tidal; EBL = estimated blood loss; IV = intravenous; CV = coefficient of variation; BIS = bispectral index.

* Step-down Bonferroni correction for multiple comparisons.

† Statistically significant at $\alpha = 0.05$.

0.0271). The requirements for phenylephrine did not differ between groups. The duration of surgery and emergence time were similar in both groups.

Duration of PACU stay was significantly shorter for patients in the DEX group (Table 4). Although patients in the DEX group had fewer hypertensive episodes (1.25 ± 1.55 vs 2.5 ± 2.0 , $P = 0.0114$), there was no difference in the number of hypertensive episodes per hour. No patients in either group required treatment for bradycardia perioperatively.

DISCUSSION

We conducted this prospective, randomized, double-blind, placebo-controlled study to examine whether an addition of DEX to a commonly administered balanced anesthetic regimen improves global hemodynamic stability in patients undergoing craniotomy. The efficacy of the anesthetic in controlling arterial blood pressure and HR intraoperatively was assessed by computing AUCs and CVs for these parameters above and below a tightly targeted hemodynamic range ($90 < \text{SBP mm Hg} < 130$, $50 < \text{HR}$

$\text{bpm} < 90$). The study demonstrated that continuous DEX infusion improved perioperative arterial blood pressure control without significantly affecting HR. We also found that intraoperative use of DEX improved hemodynamic stability in the PACU as well as shortened the PACU length of stay.

A number of antihypertensive drugs are available to treat perioperative hypertension. Labetalol is commonly used to treat hypertensive episodes in patients undergoing craniotomy, but may not be desirable in certain patient populations because of its low potency, slow onset of pick effect¹² and unpredictability in dose requirements.⁶ Esmolol is only mildly effective in treating postoperative hypertension. Its perioperative use is further complicated by bradycardia and conduction delays.¹³ Nicardipine is more effective than esmolol in controlling postoperative hypertension.¹⁴ However, it causes a dose-dependent cerebral vasodilation, inhibition of autoregulation, and a frequent incidence of hypotension (when compared with labetalol).¹⁵ Hydralazine may increase intracranial pressure by as much as 100% and is rarely used as a sole drug in treating hypertension in neurosurgical patients.¹⁶

Table 4. Postanesthesia Care Unit (PACU)

	Placebo (n = 28)		Dexmedetomidine (n = 28)		P
	Mean	SD	Mean	SD	
PACU duration (min)	130	27	91	17	<0.0001*
PACU events BP >130	2.5	2.0	1.25	1.55	0.0114*†
PACU event rate (event/h)	1.16	0.85	0.85	1.08	0.2433
	Count (%)	Median (IQR)	Count (%)	Median (IQR)	
BP Meds‡					
Any BP Med	14 (50)		10 (36)		0.2801
Labetalol	12 (43)	30 (20–40) mg	6 (21)	12.5 (10–40) mg	0.2250
Metoprolol	3 (11)	2 mg	0 (0)	NA	0.2250
Hydralazine	5 (18)	10 (5–20) mg	5 (18)	5 (5–10) mg	1.0000
Phenylephrine	4 (14)	50 (50–175) µg	0 (0)	NA	0.0379*
Analgesic Meds‡					
Any analgesic	18 (64)		15 (54)		0.4151
Morphine	7 (25)	4 mg	9 (32)	4 (2–4) mg	0.5541
Codeine	11 (39)	60 (30–60) mg	7 (25)	60 (30–60) mg	0.5048
Fentanyl	8 (29)	50 (25–50) µg	2 (7)	25 mg	0.1089
Antiemetic Meds‡					
Any antiemetic	4 (14)		2 (7)		0.3875
Ondansetron	3 (11)	4 mg	2 (7)	4 mg	1.0000
Metoclopramide	1 (4)	10 mg	0 (0)	NA	0.9389
Trimethobenzamide	2 (7)	200 mg	1 (4)	200 mg	1.0000

SD = standard deviation; BP = blood pressure; NA = not applicable.

* Statistically significant at $\alpha = 0.05$.

† Use of nonparametric test—Wilcoxon-Mann-Whitney test.

‡ Step-down Bonferroni correction for multiple comparisons.

The final common pathway leading to perioperative hypertension appears to be activation of the sympathetic nervous system, as evidenced by increased plasma catecholamine concentrations in patients after craniotomy.¹⁷ DEX decreased plasma epinephrine and norepinephrine level perioperatively.^{18,19} It is reasonable to assume that DEX would attenuate hypertensive responses associated with surgical stimulation and our pilot study corroborated this assertion.¹¹

Two studies evaluated the role of DEX in patients undergoing intracranial surgery.^{3,4} Gunes et al.³ compared perioperative hemodynamic and postanesthesia recovery profiles in patients anesthetized with DEX–remifentanyl–nitrous oxide versus propofol–remifentanyl–nitrous oxide anesthesia. Acute arterial blood pressure elevations were treated with increasing doses of propofol and DEX. No patient (in either group) required antihypertensive medication. In contrast, our experience, as well as results of other investigators, indicates that 50%–90% of neurosurgical patients require antihypertensive or vasoactive drugs.^{5,6,11} Tanskanen et al.⁴ reported, as a secondary outcome, the effect of DEX infusion (plasma concentrations 0.2 and 0.4 ng/mL) on perioperative hemodynamics in patients maintained with nitrous oxide, isoflurane, and fentanyl. They noted that SBP was outside of the targeted range of 56%, 47%, and 29% in the placebo, low DEX, and high DEX groups, respectively. Intraoperative hypertension and tachycardia (SBP >140

mm Hg, HR >100 bpm) was treated by prescribed incremental anesthetic dosing. Although we believe that a strict adherence to a study protocol is critical for initial evaluation of the drug effect, it is unlikely that complex algorithms to control arterial blood pressure would be routinely used in clinical practice. Both studies considered only the hemodynamic variables for specific time points during typically stimulating events and neither study reports a time interval that was required to reduce arterial blood pressure to the target range.

One of our main goals was to evaluate advantages (or disadvantages) of adjuvant DEX infusion in controlling perioperative hemodynamics under clinically relevant conditions. Anesthesiologists were not required to adhere to a rigid study protocol. They were responsible for treatment choices and drug dosing decisions within defined guidelines of similar depth of anesthesia, targeted hemodynamics, and rapid awakening. Analysis of continuous computerized recording allows a rigorous evaluation of anesthetic techniques based on a global assessment of hemodynamic stability, rather than comparison of arterial blood pressures and HR at single time points. The efficacy of the anesthetic technique was evaluated by calculating areas under the SBP-time and HR-time curves when these hemodynamic variables were outside the targeted window. Several studies suggest that AUC is the best

criteria to evaluate therapeutic efficacy of antihypertensive drugs.^{20,21} CVs were compared as well because two blood pressure curves may have the same AUCs but quite different shapes. CV is an index of blood pressure variability which reflects the acute hemodynamic changes, an important clinical measure in patients undergoing intracranial surgery.

With the groups not different in terms of depth of anesthesia and times to awakening and tracheal extubation, the AUCsbp (above 130 mm Hg) was significantly lower in patients treated with DEX when compared with the control group. Thus, the addition of DEX improves even the best effort of the anesthesiologist in controlling arterial blood pressure. AUCs below 90 mm Hg and 50 bpm and negative CVs for SBP and HR were not different between groups. This indicates that the addition of DEX does not lead to more intraoperative hypotension or bradycardia, which are purported complications of this drug.

There were other indicators of the DEX-related improvements of hemodynamic stability, such as significantly smaller requirements for antihypertensive drugs and intraoperative opioids. The DEX group patients demonstrated a shorter PACU stay, possibly related to fewer nursing interventions.

There are several limitations to our study. It is our usual practice, for nonemergent intracranial surgery, to place invasive arterial lines after anesthetic induction. The AUC and CV analysis, therefore, did not include the tracheal intubation time period. Also, we selected a constant DEX infusion rate of 0.5 $\mu\text{g}/\text{kg}$ after the initial loading dose of 1 $\mu\text{g}/\text{kg}$. Although we did not use targeted plasma concentrations, we selected a midrange dose with common methods of administration. As in normal clinical practice, it is possible that patients who differed in their ability to metabolize this drug received lower or higher effective doses. Factors possibly predictive of this, such as epilepsy or chronic antihypertensive medications, did not differ between the groups. It is plausible that, with a study design in which the anesthesiologist was permitted to titrate the DEX dose, further improvements in hemodynamic stability with shorter awakening times might have been demonstrated.

In conclusion, a continuous infusion of DEX improved hemodynamic stability in patients undergoing intracranial surgery without increasing the incidence of hypotensive episodes or bradycardia. In addition, patients treated with DEX were discharged from the PACU earlier than patients in the PLB group. The efficacy of the anesthetic technique in controlling hemodynamics was assessed using AUCs and CVs for SBP and HR above and below the targeted range. We believe that the analysis of continuous computerized records using global measures of hemodynamic stability is preferable to the more traditional evaluation

based on SBP and HR comparisons at the particular time-points.

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