Influence of Ventilation Strategies and Anesthetic Techniques on Regional Cerebral Oximetry in the Beach Chair Position

A Prospective Interventional Study with a Randomized Comparison of Two Anesthetics

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ABSTRACT

Background: Beach chair positioning during general anesthesia is associated with cerebral oxygen desaturation. Changes in cerebral oxygenation resulting from the interaction of inspired oxygen fraction (F_{IO_2}), end-tidal carbon dioxide (PET_{CO_2}), and anesthetic choice have not been fully evaluated in anesthetized patients in the beach chair position.

Methods: This is a prospective interventional within-group study of patients undergoing shoulder surgery in the beach chair position that incorporated a randomized comparison between two anesthetics. Fifty-six patients were randomized to receive desflurane or total intravenous anesthesia with propofol. Following induction of anesthesia and positioning, F_{IO_2} and minute ventilation were sequentially adjusted for all patients. Regional cerebral oxygenation (rS_{O_2}) was the primary outcome and was recorded at each of five set points.

Results: While maintaining F_{IO_2} at 0.3 and PET_{CO_2} at 30 mmHg, there was a decrease in rS_{O_2} from 68% (SD, 12) to 61% (SD, 12) ($P < 0.001$) following beach chair positioning. The combined interventions of increasing F_{IO_2} to 1.0 and increasing PET_{CO_2} to 45 mmHg resulted in a 14% point improvement in rS_{O_2} to 75% (SD, 12) ($P < 0.001$) for patients anesthetized in the beach chair position. There was no significant interaction effect of the anesthetic at the study intervention points.

Conclusions: Increasing F_{IO_2} and PET_{CO_2} resulted in a significant increase in rS_{O_2} that overcomes desaturation in patients anesthetized in the beach chair position and that appears independent of anesthetic choice. **(ANESTHESIOLOGY 2015; 123:765-74)**

CATASTROPHIC neurological injury following anesthesia in the beach chair position has been reported in the literature[1] and is thought to be due to cerebral hypoperfusion. Anatomic abnormalities in the Circle of Willis have been rarely discovered as the etiology,[2] and the majority of adverse events have occurred in healthy patients with recorded blood pressures that many anesthesiologists would consider acceptable.[3]

The measurement of regional cerebral oxygenation (rS_{O_2}) has been employed in routine clinical practice to detect cerebral desaturation in potential low-flow states for patients undergoing cardiac[4] and vascular surgeries.[5,6] Monitoring of rS_{O_2} in anesthetized patients undergoing surgery in beach chair position has been evaluated[7] and revealed a high incidence of cerebral desaturation ($rS_{O_2} \geq 20\%$ below baseline).[8] By measuring the relative concentrations of oxyhemoglobin and deoxyhemoglobin, cerebral near-infrared spectroscopy (NIRS) provides an estimate of the balance between cerebral oxygen supply and demand within the field of view.[9]

What We Already Know about This Topic

- Patients undergoing surgery in the beach chair position may experience cerebral oxygen desaturation, potentially sufficient to cause neurologic injury. Methods of prevention have not been proven.

What This Article Tells Us That Is New

- Cerebral oxygenation desaturation in the beach chair position, as estimated by cerebral oximetry, may be attenuated by the combination of normobaric hyperoxia and moderate hypercarbia. This appears independent of anesthetic agent.

Reports in conscious volunteers[10] and anesthetized patients without vascular disease[11] demonstrate a relationship between rS_{O_2} and both inspired oxygen fraction (F_{IO_2}) and end-tidal carbon dioxide (PET_{CO_2}). Observational data specifically captured during beach chair positioning suggest a relationship between PET_{CO_2} and rS_{O_2},[12] and in a recent randomized controlled trial, ventilation at a higher PET_{CO_2}

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was associated with higher rSo_2 values for patients anesthetized in the beach chair position.[13]

Anesthetic agents have distinct effects on cerebral hemodynamics and metabolism,[14,15] which may have implications for beach chair positioning. Agents with greater preservation of cerebral blood flow (CBF) to cerebral metabolic rate for oxygen ($CMRo_2$) ratio may allow for greater tolerance of cerebral hypoperfusion. Cerebral oxygenation appears better preserved in the beach chair position with a combination of sevoflurane–nitrous oxide compared with propofol–remifentanil,[16] yet the presence of either nitrous oxide or remifentanil could have confounded results for the primary anesthetics. In an additional study,[17] rSo_2 decreased less when using desflurane compared with propofol for the first 9 min of beach chair position, but the desflurane group received thiopental for induction, which might have also confounded the results. The effect on rSo_2 due to interactions between inspired gas composition and anesthetic choice is of clinical interest, especially when comparing propofol with desflurane, the halogenated ether with the greatest potential for cerebral vasodilatation.[18]

This study tested the hypothesis that modulation of FIo_2 and $PETco_2$ results in significant changes in rSo_2 in patients anesthetized in the beach chair position. The influence of two anesthetic techniques with distinct effects on the cerebral vasculature was tested as a secondary outcome.

Materials and Methods

A detailed description of the study protocol (ClinicalTrials.gov No. NCT01535274) has previously been published.[19] This was a prospective within-group study that incorporated a randomized comparison of two anesthetic regimens (fig. 1). The study was approved by the Institutional Review Board of the University of Michigan, Ann Arbor, and written informed consent was obtained after a detailed discussion with patients regarding risks and benefits. The primary outcome was the effect of increasing FIo_2 or $PETco_2$ on rSo_2 in patients anesthetized in the beach chair position. The secondary outcome was the effect of desflurane *versus* propofol on ventilation-related changes in rSo_2 and on cerebral desaturation in patients anesthetized in the beach chair position.

Inclusion Criteria

We recruited adult patients scheduled for elective arthroscopic shoulder surgery in the beach chair position under general anesthesia with a supplemental interscalene brachial plexus

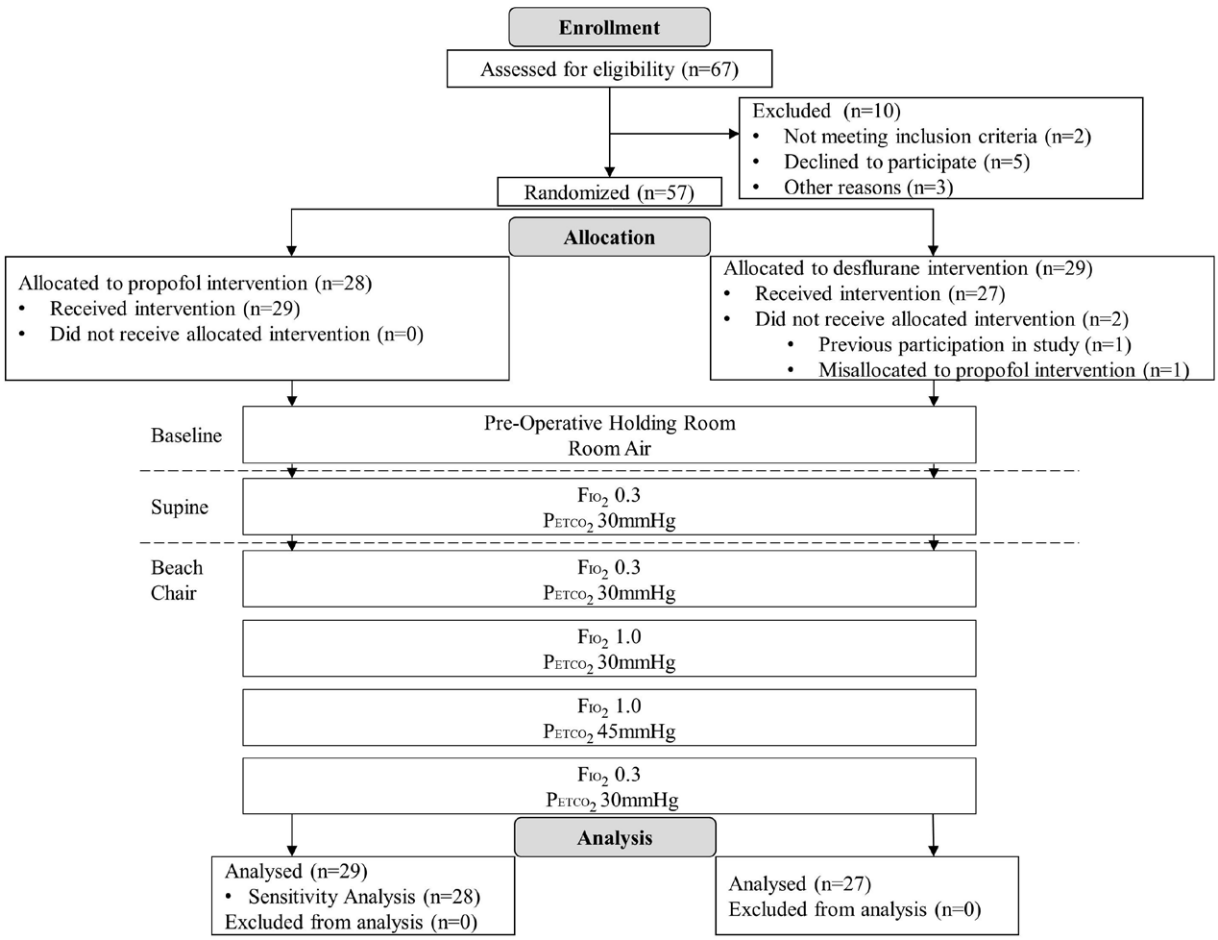

Fig. 1. Consort diagram illustrating the overall study design. FIo_2 = fraction of inspired oxygen; $PETco_2$ = partial pressure of end-tidal carbon dioxide.

block at an ambulatory surgery facility. All surgeries were conducted by a single surgeon (B.S.M.); regional and general anesthetic procedures were conducted by a single anesthesiologist (A.D.). Patients were excluded if they refused to give consent, could not speak English, had contraindications for an interscalene brachial plexus block, or had a history of cardiovascular disease, cerebrovascular disease, respiratory failure, or hypertension determined by (1) medical diagnosis, (2) the surrogate of pharmacologic treatment with an antihypertensive, or (3) a blood pressure measured in the surgical preoperative clinic of greater than 140/90.

Randomization and Blinding

Patients underwent computer-generated randomization to receive desflurane or total intravenous anesthesia with propofol for maintenance of anesthesia. These agents were chosen because of their differential effects on cerebral vasodilation, autoregulation, and carbon dioxide responsiveness.[15,20,21] Patients and data analysts were blinded to the anesthetic choice; the anesthesiologist caring for the patient was blinded to rSo_2 values. If the absolute rSo_2 was less than 55% or decreased from baseline by greater than or equal to 20%, the anesthesiologist was informed, as instructed by our Institutional Review Board.

Protocol

Baseline rSo_2 was measured in the preoperative holding area with patients sitting and breathing room air. All patients had a single-shot, ultrasound-guided, interscalene brachial plexus block performed before induction of anesthesia (20 ml of 0.5% ropivacaine). The adequacy of the block was clinically assessed using a combination of motor and sensory evaluation before proceeding to the operating room. Patients were premedicated with midazolam (0.5 to 2 mg); following preoxygenation, anesthesia was induced using fentanyl (1 to 2 μg/kg) and propofol (0.5 to 2 mg/kg). For muscle relaxation, a combination of succinylcholine and/or nondepolarizing muscle relaxants was used as was deemed clinically appropriate. The patient's trachea was intubated, the lungs were ventilated, and general anesthesia was maintained as dictated by randomization.

The primary interventions related to F_{IO_2} and minute ventilation were sequentially adjusted to the following five set points:

1. F_{IO_2} 0.3 and PET_{CO_2} 30 mmHg—supine position
2. F_{IO_2} 0.3 and PET_{CO_2} 30 mmHg—beach chair position
3. F_{IO_2} 1.0 and PET_{CO_2} 30 mmHg—beach chair position
4. F_{IO_2} 1.0 and PET_{CO_2} 45 mmHg—beach chair position
5. F_{IO_2} 0.3 and PET_{CO_2} 30 mmHg—beach chair position

The initial tidal volume was set at 6 to 8 cc/kg body weight and minute ventilation adjusted first by changing respiratory rate rather than manipulating tidal volume. Blood pressure was recorded by noninvasive cuff placed on the nonoperative arm. No correction factor was applied to account for the difference in vertical height between the blood pressure measurement site and the Circle of Willis. All patients were placed at 80 to 90° in the beach chair position depending on body habitus. The surrogate for depth of anesthesia was the bispectral index (BIS; Covidien, USA), which was targeted to the range of 40 to 60. Nitrous oxide could potentially confound results and was therefore avoided. The first measurement in the beach chair position (set point two) was obtained either 15 min after positioning, allowing the maximal decrease in rSo_2 to occur,[8] or immediately if cerebral desaturation (defined as an absolute rSo_2 value < 55% or a decrease from baseline of ≥ 20%) was sustained for more than or equal to 3 min in either hemisphere. Since the change in rSo_2 is typically complete and stable within 5 min following a change in inspired gas composition,[5] rSo_2 was recorded as a "snap shot" after a minimum of 5 min at each subsequent set point. All cerebral desaturation events (absolute rSo_2 value < 55% or a decrease from baseline of ≥ 20% sustained for ≥ 3 min) were recorded and communicated by the clinical coordinator to allow intervention as deemed appropriate by the anesthesiologist: exclude and treat hypotension, exclude and treat excessive depth of anesthesia, and move to the next ventilation set point if that included increasing F_{IO_2} or PET_{CO_2}. If cerebral desaturation occurred moving from set point 4 to set point 5, rSo_2 was recorded before full equilibrium had been reached and F_{IO_2} and/or PET_{CO_2} were increased. Hematocrit was measured at the beginning and end of the study period (set point 1 and set point 5). Demographic and intraoperative data were retrieved from the patient's electronic anesthetic and medical records.

Blood pressure management has been detailed in the published protocol.[19] Briefly, either ephedrine (5 mg) and/or phenylephrine (50 to 100 μg) were used as intravenous bolus medications for the treatment of intraoperative hypotension. If bolus dose phenylephrine was used first, we delayed the recording of results following a trial intervention by at least 8 min in order to allow rSo_2 to normalize.[22] For patients requiring more than 400 μg of phenylephrine during a 20-min period, phenylephrine by infusion (200 μg/ml) was titrated to maintain blood pressure within 20% of preoperative mean arterial pressure (MAP).

Standard American Society of Anesthesiologists monitoring was used for all patients. The BIS Quatro electrode was placed diagonally on the patient's left forehead. rSo_2 was measured using the INVOS 5100C monitor (Covidien, USA). Before induction of anesthesia, a single trained researcher applied optodes to either side of the forehead in conjunction with the BIS Quatro sensor as recommended by the manufacturer.

Sample Size and Statistical Analysis

The reported mean rSo_2 is 67.1 ± 6.2% for patients placed in beach chair position.[8] Based on a previous investigation,[11] we expected a 6 to 8% point difference in rSo_2 due to the planned change in F_{IO_2} and a 2 to 4% point difference due to the planned change in PET_{CO_2}. A total percentage point increase in excess of 10 was prespecified[19] as an outcome of clinical relevance. A sample size of 24 has a power of greater

than 0.8 to detect a 4 to 5% increase in the planned pairwise comparisons related to the primary intervention of ventilation strategy. The power for the comparison between the two anesthetic regimens (48 subjects) is better than 85% for a difference of 6%, which was prespecified[19] as a clinically important difference for the secondary outcome.

Data were analyzed with repeated-measures ANOVA with ventilation strategy as the within-subjects factor (primary outcome) and anesthetic regimen as the between-subjects factor (secondary outcome). Residuals were assessed for normality and equal variances. A *post hoc* Tukey honest significant difference procedure was used to correct for all pairwise comparisons between ventilation strategies. All analyses were performed using SPSS version 21.0 (SPSS Inc., USA). A *P* value of less than 0.05 was considered statistically significant.

Results

Study Populations

Fifty-six patients were recruited and none were withdrawn (fig. 1); all patients tolerated their procedure and recovered without complication. Twenty-eight patients were randomized to receive propofol and 28 patients were randomized to receive desflurane; secondary to the misallocation of one patient, 29 patients received propofol and 27 patients received desflurane. All patients had a functional brachial plexus block before leaving the preoperative holding area. None required supplementation with additional local anesthesia. There were no significant differences in patient characteristics or baseline data between groups (table 1). When patients were awake and breathing room air, the mean rSo_2

Table 1. Patient Characteristics and Baseline Data

	Propofol (n = 29)	Desflurane (n = 27)	
	n (%)	n (%)	*P* Value*
Sex			
Female	11 (37.9)	10 (37.0)	0.945
Male	18 (62.1)	17 (63.0)	
ASA physical status			
1	8 (27.6)	6 (22.2)	0.899
2	20 (69.0)	20 (74.1)	
3	1 (3.4)	1 (3.7)	
BMI category†			
Normal (18.5–24.9)	7 (24.1)	4 (14.8)	0.176
Overweight (25.0–29.9)	14 (48.3)	9 (33.3)	
Obese (≥30.0)	8 (27.6)	14 (51.9)	
Smoking status			
Nonsmoker	23 (79.3)	19 (70.4)	0.419
Previous smoker	4 (13.8)	3 (11.1)	
Current smoker	2 (6.9)	5 (18.5)	
Comorbidities			
Sleep apnea	8 (27.6)	5 (18.5)	0.422
Hypercholesterolemia	5 (17.2)	2 (7.4)	0.424
Asthma/COPD	7 (24.1)	3 (11.1)	0.299
Diabetes	1 (3.4)	0	1.000
Heart disease	0	0	NA
Medications			
β-adrenergic blockers	0	1 (3.7)	0.482
Calcium channel blockers	2 (6.9)	2 (7.4)	1.000
ACE inhibitors	0	0	NA
Angiotensin receptor blockers	0	0	NA
Diuretics	0	0	NA
	Mean (SD)	Mean (SD)	*P* Value*
Age (yr)	51.3 (10.0)	49.3 (13.3)	0.524
Baseline systolic blood pressure	124.3 (15.4)	123.2 (11.7)	0.775
Baseline diastolic blood pressure	74.8 (8.3)	73.0 (9.1)	0.432
Baseline left rSo_2	71.0 (13.0)	70.3 (11.4)	0.831
Baseline right rSo_2	69.1 (11.3)	68.4 (9.8)	0.798

* *P* values calculated using Pearson chi-square or Fisher exact test as appropriate for categorical variables and a *t* test for continuous variables. † BMI categories based on World Health Organization classification.

ACE = angiotensin-converting enzyme; ASA = American Society of Anesthesiologists; BMI = body mass index; COPD = chronic obstructive pulmonary disease; NA = not applicable; rSO_2 = regional cerebral oxygen saturation.

on the left was 71%, SD 13, and on the right was 69%, SD 11. There was no significant difference in rSo_2 between operative and nonoperative sides at any of the measurement points. There were three outliers, one in the desflurane group and two in the propofol group, who displayed mean room air rSo_2 between 36 and 40%; none of the study or clinical interventions achieved a clinically meaningful increment in rSo_2 in these patients. All patients were included for complete analysis.

Influence of Beach Chair Positioning on rSo_2

While maintaining FIo_2 at 0.3 and $PETco_2$ at 30 mmHg, there was a decrease in rSo_2 from 68% (SD, 12) to 61% (SD, 12) ($P < 0.001$) following beach chair positioning when compared with stable supine patients with the same ventilation parameters for the combined data set (table 2).

Influence of Ventilation Strategy on rSo_2

The overall repeated-measures ANOVA, including the first five set points, revealed that ventilation strategy had a significant within-subjects effect on rSo_2 ($P < 0.001$). While maintaining $PETco_2$ at 30 mmHg, rSo_2 improved by 5% points when FIo_2 1.0 was delivered compared with FIo_2 0.3 (mean, 66%; SD, 12 *vs.* mean, 61%; SD, 12; $P < 0.001$). At 1.0 FIo_2, an additional 9% point improvement was observed at $PETco_2$ 45 mmHg when compared with $PETco_2$ 30 mmHg (mean, 75%; SD, 12 *vs.* mean, 66%; SD, 12; $P < 0.001$). A total increment of 14% points was achieved comparing FIo_2 0.3 and $PETco_2$ 30 mmHg (mean, 61%; SD, 12) with FIo_2 1.0 and $PETco_2$ 45 mmHg (mean, 75%; SD, 12) in the beach chair position ($P < 0.001$). This value is also 7% points higher than that measured in supine anesthetized patients at FIo_2 0.3 and $PETco_2$ 30 mmHg (mean, 75%; SD, 12 *vs.* mean, 68%; SD, 12; $P < 0.001$). With the exception of the three outliers, all patients responded consistently to the changes in ventilation strategy with the same direction of change in rSo_2. Table 2 summarizes the rSo_2 during the trial interventions for the combined sample and for each anesthetic choice. Figure 2 illustrates the percentage change from baseline rSo_2.

Influence of Anesthetic Regimen on rSo_2

There was no significant interaction effect of the anesthetic on rSo_2 as a between-subjects factor at the study intervention points. Ten patients in the propofol group and nine in the desflurane group exhibited rSo_2 less than 55% or a decrease from baseline of greater than or equal to 20% sustained for more than or equal to 3 min in either hemisphere, necessitating an early increase in FIo_2 to 1.0 during the first 15 min following beach chair positioning. There was no statistically significant difference in cerebral desaturation rate between groups.

Controlling for BIS Values, Anesthetic Concentrations, Hemodynamics, and Hematocrit

The mean time interval between interventions 1 and 2 was 16 min (SD, 5), between 2 and 3 was 10 min (SD, 3), between 3 and 4 was 12 min (SD, 3), and between 4 and 5 was 10 min (SD, 2). The mean BIS at each study intervention point was held within two points of the lower limit of our target range (40) for the combined sample (table 3). There was no difference in BIS as a between-subjects factor when comparing the propofol and desflurane groups. There was no statistically significant change in either propofol infusion rate or end-tidal desflurane throughout the study (table 4). There was no statistically significant change in systolic or diastolic blood pressure throughout the intervention period in either the propofol or desflurane groups. There was no statistically significant difference in systolic blood pressure during the intervention period seen between the propofol and desflurane groups, but the diastolic blood pressure was consistently and significantly lower in the desflurane group when analyzed as a between-subjects factor ($P = 0.001$) (fig. 3). The mean difference seen in diastolic blood pressure throughout the intervention period was 11 mmHg. There was no significant variation in heart rate throughout the intervention period, but heart rate was consistently lower in the desflurane group, mean 77 (propofol) *versus* 65 (desflurane) beats/min ($P = 0.002$) (fig. 4). There was no significant difference in the number of patients receiving ephedrine as a bolus medication (8 [propofol] *vs.* 10 [desflurane]), the total number of doses (14 [propofol]

Table 2. Regional Cerebral Oxygenation Values (Mean ± SD) at the Set Ventilatory Points of the Study for the Study Group and for Each Anesthetic Choice

	Supine	Beach Chair			
	Set Point 1	Set Point 2	Set Point 3	Set Point 4	Set Point 5
	FIo_2 0.3; $PETco_2$ 30 mmHg	FIo_2 0.3; $PETco_2$ 30 mmHg	FIo_2 1.0; $PETco_2$ 30 mmHg	FIo_2 1.0; $PETco_2$ 45 mmHg	FIo_2 0.3; $PETco_2$ 30 mmHg
Combined (n = 56)	68 ± 12	61 ± 12 ($P < 0.001$)	66 ± 12 ($P < 0.001$)	75 ± 12 ($P < 0.001$)	65 ± 13 ($P < 0.001$)
Propofol (n = 29)	67 ± 13	59 ± 13 ($P < 0.001$)	64 ± 14 ($P < 0.001$)	74 ± 12 ($P < 0.001$)	64 ± 14 ($P < 0.001$)
Desflurane (n = 27)	69 ± 11	62 ± 10 ($P < 0.001$)	67 ± 11 ($P < 0.001$)	76 ± 11 ($P < 0.001$)	67 ± 12 ($P < 0.001$)

P values represent comparison of successive set points within anesthetic type (*i.e.*, Set Point 1 compared to Set Point 2, Set Point 2 compared to Set Point 3, *etc.*).

FIo_2 = fraction of inspired oxygen; $PETco_2$ = partial pressure of end-tidal carbon dioxide.

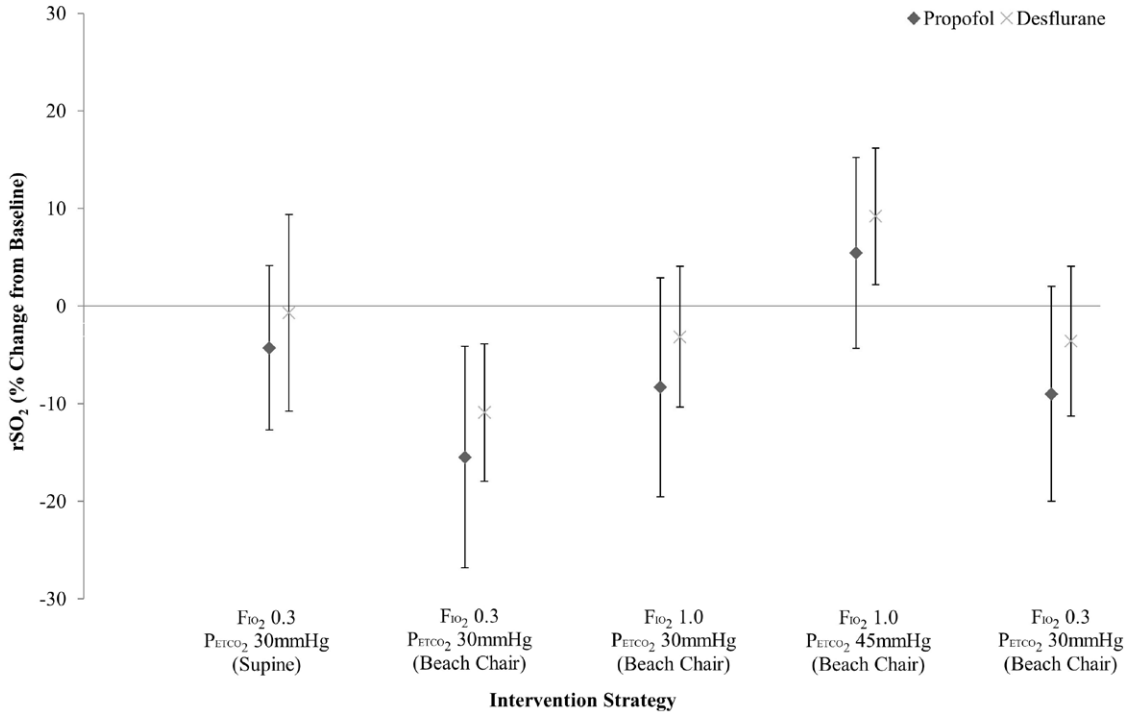

Fig. 2. Percentage change from baseline regional cerebral oxygenation (rSo_2) at each study point for propofol and desflurane groups. FIO_2 = fraction of inspired oxygen; $PETCO_2$ = partial pressure of end-tidal carbon dioxide.

Table 3. BIS Values (Mean ± SD) at the Set Ventilatory Points of the Study for the Study Group and for Each Anesthetic Choice

	Supine	Beach Chair			
	Set Point 1	Set Point 2	Set Point 3	Set Point 4	Set Point 5
	FIO_2 0.3; $PETCO_2$ 30 mmHg	FIO_2 0.3; $PETCO_2$ 30 mmHg	FIO_2 1.0; $PETCO_2$ 30 mmHg	FIO_2 1.0; $PETCO_2$ 45 mmHg	FIO_2 0.3; $PETCO_2$ 30 mmHg
Combined (n = 56)	38 ± 10	41 ± 11 (P = 0.04)	39 ± 9 (P = 0.15)	42 ± 8 (P = 0.04)	39 ± 8 (P = 0.01)
Propofol (n = 29)	42 ± 11	42 ± 13 (P = 0.86)	40 ± 11 (P = 0.23)	42 ± 10 (P = 0.18)	41 ± 10 (P = 0.27)
Desflurane (n = 26)*	34 ± 7	40 ± 8 (P = 0.04)	39 ± 4 (P = 0.40)	41 ± 6 (P = 0.03)	38 ± 5 (P < 0.01)

P values represent comparison of successive set points within anesthetic type (*i.e.*, Set Point 1 compared to Set Point 2, Set Point 2 compared to Set Point 3, *etc.*).

* One patient with missing BIS data.

BIS = bispectral index; FIO_2 = fraction of inspired oxygen; $PETCO_2$ = partial pressure of end-tidal carbon dioxide.

Table 4. Propofol Infusion (Mean ± SD) and End-tidal Desflurane (Mean ± SD) at the Set Ventilatory Points

	Supine	Beach Chair			
	Set Point 1	Set Point 2	Set Point 3	Set Point 4	Set Point 5
	FIO_2 0.3; $PETCO_2$ 30 mmHg	FIO_2 0.3; $PETCO_2$ 30 mmHg	FIO_2 1.0; $PETCO_2$ 30 mmHg	FIO_2 1.0; $PETCO_2$ 45 mmHg	FIO_2 0.3; $PETCO_2$ 30 mmHg
Propofol infusion rates (n = 29), μg kg^{-1} min^{-1}	108.8 ± 25.5	115.9 ± 16.4	114.7 ± 17.3	112.2 ± 17.3	108.7 ± 19.4
End-tidal desflurane (n = 27), %	4.4 ± 0.9	4.7 ± 0.8	4.8 ± 0.8	4.6 ± 0.8	5.0 ± 0.7

FIO_2 = fraction of inspired oxygen; $PETCO_2$ = partial pressure of end-tidal carbon dioxide.

vs. 18 [desflurane]), or the total dose (70 mg [propofol] *vs.* 90 mg [desflurane]), administered during the study period to each of the anesthetic groups when considered as entire groups. There was no significant difference in the number of patients receiving phenylephrine as a bolus medication (five in the propofol group and seven in the desflurane group

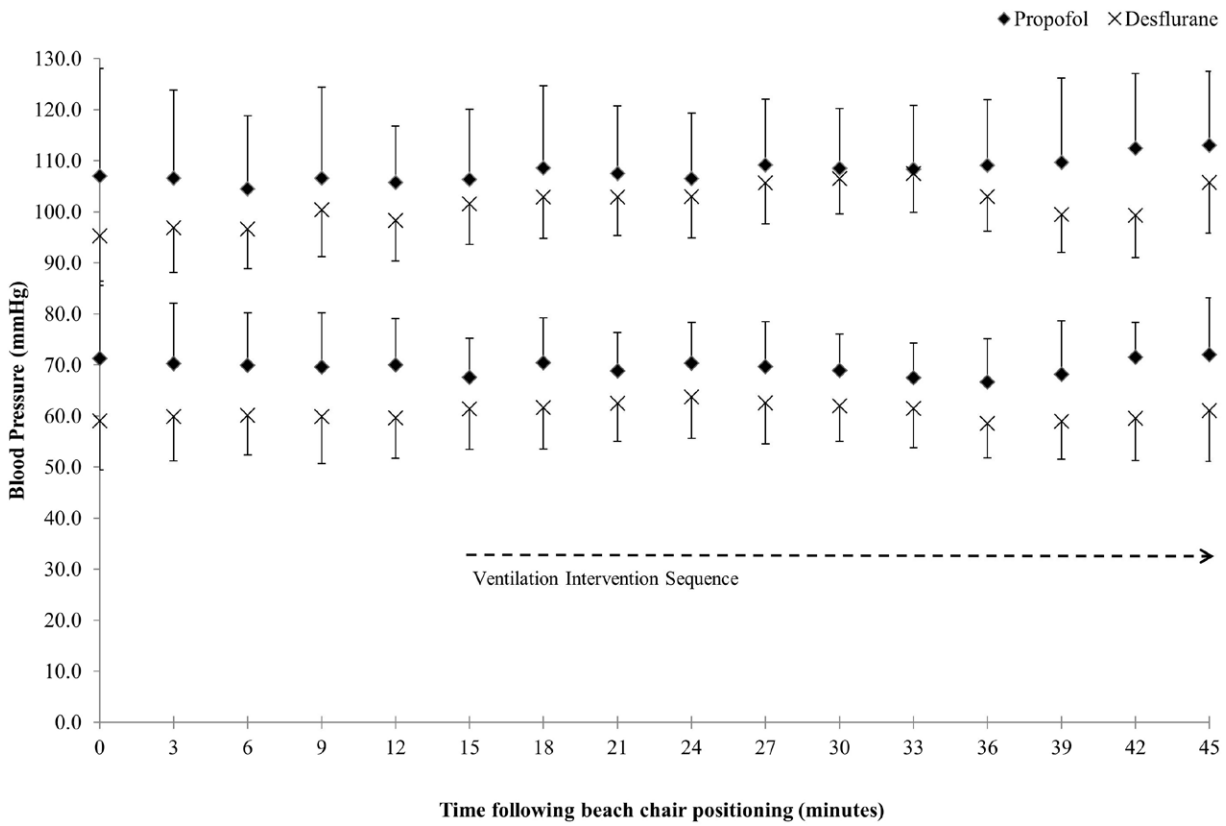

Fig. 3. Mean systolic and diastolic blood pressure, with 1 SD, throughout the intervention period for the propofol and desflurane groups.

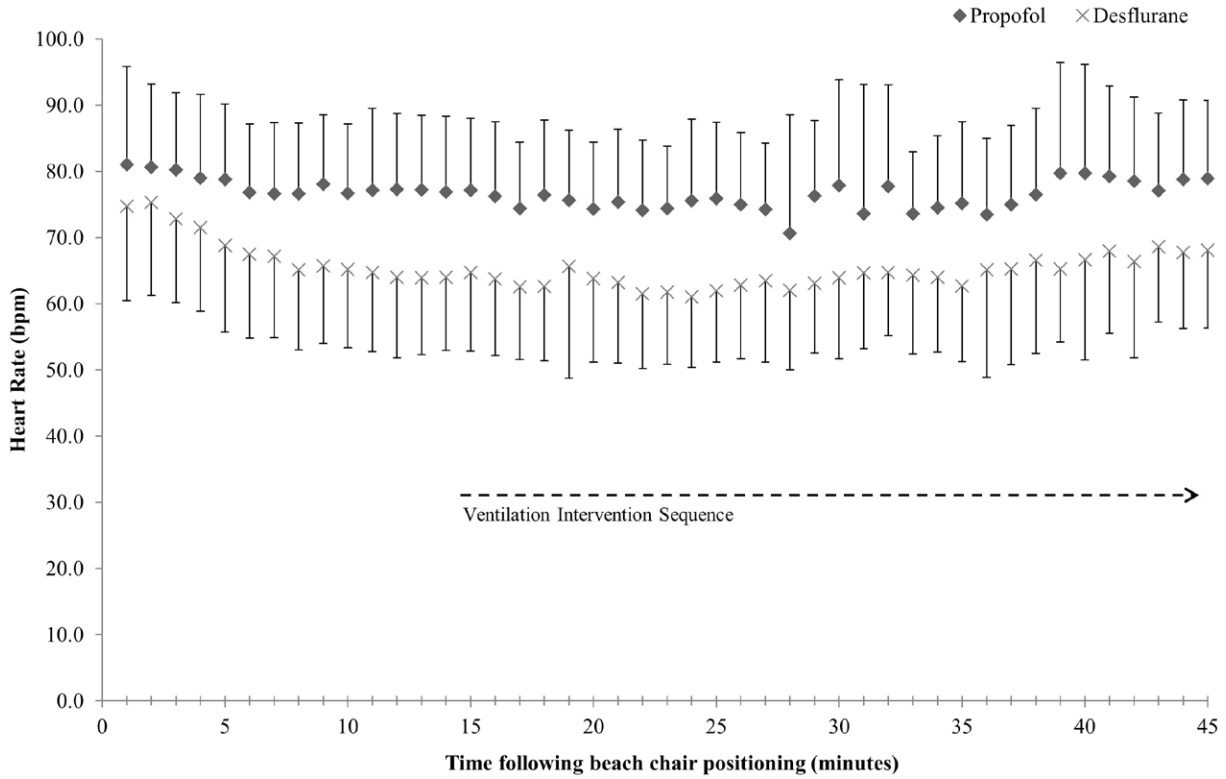

Fig. 4. Mean heart rate, with 1 SD, throughout the study period for propofol and desflurane groups. bpm = beats/min.

within the intervention period). The total number of phenylephrine doses (17 *vs.* 31) and the total dose (1,000 *vs.* 1,800 mg) administered to each group throughout the study period were both significantly higher in the desflurane group ($P < 0.01$). No patient required phenylephrine by infusion. There was a statistically significant difference between hematocrit measured at set point 1 (median, 43; interquartile range, 38 to 46) and set point 5 (median, 41; interquartile range, 38 to 44; $P = 0.001$).

Sensitivity Analysis

The misallocation carried the potential to impact the results of the secondary outcome; one patient in the propofol group was excluded from the sensitivity analysis of the remaining 55 patients (28 in the propofol group and 27 in the desflurane group). The analysis revealed no significant differences compared to the full study population. As in the complete cohort, the increase in F_{IO_2} and PET_{CO_2} resulted in a significant increase in rSo_2 ($P < 0.001$ for comparisons of each consecutive set point), which was independent of anesthetic choice ($P = 0.513$).

Discussion

The results of this dynamic interventional study demonstrate that simple modulation of inspired gas composition leads to an elevation in rSo_2 for patients anesthetized in the beach chair position. The magnitude (14% points) of the combined intervention not only increased rSo_2 but did so to a level surpassing that measured in the supine position. The relative increments seen with increasing F_{IO_2} and PET_{CO_2} were 5 and 9% points, respectively. Except for three outliers who demonstrated low baseline cerebral saturations, the responses were consistent throughout our study population. The results are not only highly statistically significant but also have exceeded our prespecified threshold for clinical relevance.[19] The data can help guide the clinical management of patients anesthetized in the beach chair position and prioritize interventions for the treatment of cerebral desaturation. Our results also demonstrate that ventilation strategy is a more powerful intervention to improve rSo_2 than anesthetic choice. In this study, there was no significant interaction effect of the two anesthetics studied as a between-subjects factor at the study intervention points. The lack of an anesthetic effect in our research is a potentially generalizable observation, given the relative effects of propofol and desflurane on CBF:$CMRo_2$ ratio.

It is important to note that the functional relevance of rSo_2 changes was not evaluated in this study, and the risk of cerebrovascular compromise with beach chair positioning is unclear. Overt stroke was not reported in a retrospective evaluation of more than 5,000 patients anesthetized in the sitting position. The intraoperative MAP of that population was maintained at approximately 75 mmHg or greater.[23] However, the interpretation of this value is problematic because cerebral autoregulation is attenuated (CBF becomes more dependent on systemic blood pressure) with a wide range of MAP at the lower limit of autoregulation[24] during anesthesia in the beach chair position. Until the lower limit of autoregulation can be routinely monitored, blood pressure control alone cannot be assumed sufficient to protect patients from neurological injury during anesthesia in the beach chair position.

The modulation of inspired gas composition has been previously shown to improve cerebral oxygenation measured by NIRS in awake subjects,[10] in healthy supine anesthetized patients,[11] and in patients undergoing carotid endarterectomy with either general or regional anesthesia.[5,6] Increasing F_{IO_2} during carotid endarterectomy with regional anesthesia has also been reported to reverse neurological deficits seen with carotid cross clamp placement.[25] Our results are consistent with these data as well as with findings from the static comparison of two PET_{CO_2} ranges in the beach chair position[13]; rSo_2 was better preserved with fewer cerebral desaturation events at the higher PET_{CO_2} range. However, our study advances the field by demonstrating that interventions related to carbon dioxide can help reverse decreases in rSo_2 in the beach chair position, supporting a causal influence. The partial pressure of arterial carbon dioxide (Pa_{CO_2}) is a direct determinant of CBF[26]; the impact on cerebral autoregulation remains to be fully elucidated. The combination of hypocapnia and hypotension is particularly associated with cerebral desaturation, as measured by NIRS, during anesthesia in the beach chair position.[13]

The measurement of cerebral oxygenation by NIRS and its application to patients anesthetized in the beach chair position remain controversial. There is wide intersubject variability, but a change is considered to be of greater significance than baseline readings.[9] Reductions below 50% absolute value[27,28] and reductions of greater than or equal to 20% from baseline[29–32] have been associated with cerebral ischemia. Reductions of similar magnitude have been measured in patients placed in the beach chair position using the INVOS[12] and FORE-SITE[13] (CASMED, USA) series of cerebral oximeters but was not detected when NIRO instruments (Hamamatsu, Japan) have been used[33] in this context. As the three outliers from our study demonstrate, patients may exhibit rSo_2 below 50% or exhibit a reduction of greater than or equal to 20% from baseline without any other correlate of cerebral ischemia. The INVOS system is susceptible to extracranial signal contamination,[34] but data gained during sequential clamping of the external and internal carotid artery suggest that the signal is predominantly intracranial in origin.[35] Near-infrared light penetrates the gray matter by a few millimeters,[36] and therefore, oxygenation is measured only in the superficial cortex. Cerebral oximetry values are impacted by systemic blood pressure,[37] sensor location,[38] anesthetic depth for vapor-based anesthetic techniques,[39] and hematocrit.[38] The cerebral a:v ratio is assumed constant within device algorithms, and therefore, rSo_2 can vary without a true change in cerebral oxygenation.

When making a choice between general anesthetic agents for patients with potential cerebral hypoperfusion, the balance between cerebral blood supply and oxygen demand is

of logical importance. In our study, statistical significance was not achieved for any difference relating to anesthetic choice, but this potentially relates to the particular monitor used. Differences in cerebral saturation measured by an alternative methodology may have been detected. It is interesting to note that diastolic blood pressure and heart rate were consistently lower within the desflurane group and that, although a similar number of patients within both anesthetic groups required bolus dose ephedrine and phenylephrine, the total number of doses and the total dose of phenylephrine were higher in the desflurane group. Per the study protocol, measurements were avoided following phenylephrine bolus medication to avoid the potentially confounding effect on rSo_2 seen with this drug. However, differences in hemodynamic control between the two groups may have confounded the comparison between anesthetic methodologies. There are insufficient data to help estimate the potential change in rSo_2 caused by heart rate. Diastolic blood pressure shows positive correlation, approximately 1 to 2% per 10 mmHg, with cerebral oximetry in congestive heart failure.[40] It is possible that a similar relationship exists in patients without heart failure or those in the beach chair position, but this has not been determined.

There are a number of limitations to this study. The anesthesiologist was informed of cerebral desaturation when it occurred, thus allowing for protocol modification that may have impacted the results. The measured lower level of rSo_2 with beach chair positioning was potentially limited, and therefore, we may have underestimated the magnitude of the response subsequent to increasing Fio_2 and $PETco_2$. We waited for stability in rSo_2 following manipulation of ventilation and inspired oxygen before recording, with a mean time between measurements of 10 min or greater, but it is possible that brain equilibrium was not complete at the time of data measurement. More precise reporting of respiratory gases and blood pressure could have been facilitated by the placement of intra-arterial catheters. A small number of active smokers and patients with airway disease were included; $PETco_2$ may not have reliably reflected $Paco_2$ in these patients. However, we have demonstrated predictable increments in both Pao_2 and $Paco_2$ with similar inspired gas modulation in previous studies,[6] and for healthy individuals, $PETco_2$ provides a reliable estimate of $Paco_2$.[41] Invasive blood pressure measurement with the transducer zeroed at the level of the Circle of Willis would have compensated for differences in patient height and the angle of beach chair placement (which could have confounded the secondary outcome) and would have allowed better appreciation of changes in cerebral perfusion pressure. Our initial plan[19] involved the measurement of hematocrit at each set point. This proved practically difficult during the first few subjects so the protocol was amended to include a hematocrit check at points 1 and 5 only. It is possible that the small statistically significant negative change in hematocrit (median, 43 to 41) during the entire study period blunted the effect of our interventions designed to improve rSo_2,[38] but the impact in all likelihood is clinically negligible. Unmeasured potential confounders include cerebral a:v ratio and $CMRo_2$, which present major challenges for data interpretation based on cerebral NIRS methodology.

In conclusion, increasing Fio_2 and $PETco_2$ resulted in a reliable and measurable increase in rSo_2 that overcame cerebral desaturation associated with general anesthesia in the beach chair position. Furthermore, ventilation strategy had a greater influence on rSo_2 than choice of anesthetic.

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Competing Interests

The authors declare no competing interests.

Reproducible Science

Full protocol available at: ppicton@med.umich.edu. Raw data available at: ppicton@med.umich.edu.

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