Effect of ventilation on cerebral oxygenation in patients undergoing surgery in the beach chair position: a randomized controlled trial

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Editor’s key points
- Anaesthesia in the beach chair position commonly causes systemic hypotension.
- It may also reduce cerebral blood flow (CBF) and oxygenation.
- Hypocarbia reduces CBF and oxygen delivery.
- The authors report fewer cerebral desaturation events when ventilation is adjusted to achieve $\text{ETCO}_2$ of 40–42 mm Hg when compared with 30–32 mm Hg.

Background. Surgery in the beach chair position (BCP) may reduce cerebral blood flow and oxygenation, resulting in neurological injuries. The authors tested the hypothesis that a ventilation strategy designed to achieve end-tidal carbon dioxide ($\text{ETCO}_2$) values of 40–42 mm Hg would increase cerebral oxygenation ($\text{SctO}_2$) during BCP shoulder surgery compared with a ventilation strategy designed to achieve $\text{ETCO}_2$ values of 30–32 mm Hg.

Methods. Seventy patients undergoing shoulder surgery in the BCP with general anaesthesia were enrolled in this randomized controlled trial. Mechanical ventilation was adjusted to maintain an $\text{ETCO}_2$ of 30–32 mm Hg in the control group and an $\text{ETCO}_2$ of 40–42 mm Hg in the study group. Cerebral oxygenation was monitored continuously in the operating theatre using near-infrared spectroscopy. Baseline haemodynamics and $\text{SctO}_2$ were obtained before induction of anaesthesia, and these values were then measured and recorded continuously from induction of anaesthesia until tracheal extubation. The number of cerebral desaturation events (CDEs) (defined as a ≥ 20% reduction in $\text{SctO}_2$ from baseline values) was recorded.

Results. No significant differences between the groups were observed in haemodynamic variables or phenylephrine interventions during the surgical procedure. $\text{SctO}_2$ values were significantly higher in the study 40–42 group throughout the intraoperative period ($P<0.01$). In addition, the incidence of CDEs was lower in the study 40–42 group (8.8%) compared with the control 30–32 group (55.6%, $P<0.0001$).

Conclusions. Cerebral oxygenation is significantly improved during BCP surgery when ventilation is adjusted to maintain $\text{ETCO}_2$ at 40–42 mm Hg compared with 30–32 mm Hg.

Clinical trial registration. ClinicalTrials.gov NCT01546636.

Keywords: patient positioning; spectroscopy, near-infrared; ventilation

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tissue (frontal cortex). Oxygenated and deoxygenated haemoglobin have different absorption spectra, and regional oxygen saturation in cerebral tissue can be determined by measuring the differential absorption of light as it passes through a curvilinear path from the light sources to the detectors. Studies have demonstrated that \( \text{ScO}_2 \) measured with NIRS is concordant with CBF variations when arterial oxygen saturation and cerebral oxygen consumption are constant. Previous investigations have used NIRS technology to determine changes in \( \text{ScO}_2 \) during shoulder surgery in the BCP. A high incidence (80%) of cerebral desaturation events (CDEs, most commonly defined as a decrease in \( \text{ScO}_2 \) values of >20% from baseline values) has been observed during BCP shoulder surgery under general anaesthesia with controlled ventilation and hyperventilation. In contrast, a low incidence of CDE (0–10%) has been noted in patients undergoing the same procedure with regional anaesthesia, sedation, and spontaneous ventilation.

Studies in supine awake volunteers and surgical patients have demonstrated that changes in ventilation and end-tidal carbon dioxide tension \( (\text{ETCO}_2) \) result in significant alterations in \( \text{ScO}_2 \) values. During BCP surgery, postural decreases in \( \text{ScO}_2 \) were related to both arterial pressure and \( \text{ETCO}_2 \). When general anaesthesia is used for BCP shoulder surgery, patients are frequently intubated and hyperventilated, this common practice may increase the risk of CDE. The aim of this investigation was to assess the impact of two different ventilation strategies on cerebral oxygenation during BCP surgery (standard clinical practice of hyperventilation compared with normoventilation). Patients were randomized to a control 30–32 group (standard practice-ventilated to an \( \text{ETCO}_2 \) of 30–32 mm Hg) or a study 40–42 group (ventilated to an \( \text{ETCO}_2 \) of 40–42 mm Hg), and the effect of ventilation strategy on intraoperative \( \text{ScO}_2 \) values, the incidence of CDEs, and clinical recovery were determined. The relationship between hyperventilation, hypotension, and \( \text{ScO}_2 \) was also examined.

**Methods**

**Study population and anaesthetic management**

This randomized controlled trial was approved by the North-Shore University HealthSystem Institutional Review Board (Evanston, IL, USA) and registered at ClinicalTrials.gov (NCT01546636). Written informed consent was obtained from all patients. Seventy ASA physical status I–III patients undergoing elective shoulder arthroscopy in the BCP under general anaesthesia with controlled ventilation were enrolled. All patients were operated on by a single surgeon, and regional anaesthesia was not used (as either part of an intraoperative anaesthetic or for postoperative pain management). Exclusion criteria included: age <18 or >80 yr; orthostatic hypotension or poorly controlled hypertension; pre-existing history of cerebrovascular disease or pulmonary disease; and symptomatic cardiovascular disease.

Patients were allocated randomly to one of the two groups using a computer-generated randomization code. The individual randomization assignments were concealed in opaque envelopes until the patients entered the operating theatre.

Patients in the control group were assigned a ventilation strategy designed to achieve an \( \text{ETCO}_2 \) of 30–32 mm Hg throughout the intraoperative period. This \( \text{ETCO}_2 \) concentration reflects average values observed in our clinical practice (in an observational pilot study of 20 patients) and in several academic and private practices in Illinois. Patients in the study group were assigned to a ventilation strategy with the goal of maintaining \( \text{ETCO}_2 \) values of 40–42 mm Hg. Clinicians providing intraoperative care were not blinded to group assignment. Patients, researchers, and clinicians administering postoperative care were blinded to group assignment.

Anaesthetic management was standardized in both study groups. Intraoperative monitoring consisted of electrocardiography, pulse oximetry, capnography, bispectral index monitoring (BIS™ system, Aspect Medical Systems, Newton, MA, USA), and systemic arterial pressure via an automatic arterial pressure cuff (measurement interval every 2 min, or more frequently if clinically required) on the non-operative upper extremity.

Anaesthetic induction consisted of propofol 2 mg kg\(^{-1}\), fentanyl 100 \( \mu \)g, and rocuronium 0.6–0.8 mg kg\(^{-1}\). Anaesthesia was maintained with sevoflurane 1.0–3.0% in an oxygen/air mixture [fraction of inspired oxygen (\( \text{FiO}_2 \)) of 50%]. The sevoflurane concentration was adjusted to achieve BIS values of 40–60 and to maintain mean arterial pressure (MAP) within 20% of baseline values. Approximately 1–2 mg kg\(^{-1}\) h\(^{-1}\) of fentanyl was administered intraoperatively. Ondansetron was administered 30 min before the anticipated completion of the surgical procedure. Neuromuscular block was antagonized with neostigmine 50 \( \mu \)g kg\(^{-1}\) and glycopyrrolate 10 \( \mu \)g kg\(^{-1}\) when a train-of-four count of 3–4 was present.

In the control 30–32 group, an initial tidal volume of 8 cc kg\(^{-1}\) was established immediately after tracheal intubation. Respiratory rate was adjusted to achieve \( \text{ETCO}_2 \) concentrations of 30–32 mm Hg. In the study 40–42 group, the same tidal volume and gas mixture were used, but respiratory rate was adjusted to attain an \( \text{ETCO}_2 \) of 40–42 mm Hg. End-tidal carbon dioxide concentrations were monitored and recorded continuously in the operating theatre, and respiratory rate was adjusted to achieve appropriate \( \text{ETCO}_2 \) targets.

Per protocol, hypotension (defined as a ≥20% decrease in MAP from baseline values obtained on admission to the operating theatre) was treated with a bolus dose of phenylephrine (80 \( \mu \)g). The measured systemic arterial pressure was uncorrected for gravitational gradients. Additional doses of phenylephrine were administered until target arterial pressure goals were met.

**Cerebral oxygenation measurements and perioperative data collection**

Cerebral oxygenation was monitored continuously in operating theatre using the FORE-SIGHT system (CAS Medical Systems Inc., Branford, CT, USA). The FORE-SIGHT device is a continuous wave, spatially resolved cerebral oximeter that uses four discrete wavelengths of laser light to calculate \( \text{ScO}_2 \) values. Sensors were applied bilaterally to each fronto-temporal area after cleansing the skin with alcohol. The cerebral oximetry and
BIS® probes were placed in the preoperative holding area and covered with an opaque towel to prevent light interference.

Baseline heart rate (HR), MAP, peripheral oxygen saturation (SpO₂), and SctO₂ were obtained before induction of anaesthesia. Initial values were obtained while patients were breathing a 50% inspired oxygen gas mixture via a face mask (similar to intraoperative gas mixture). Baseline data were downloaded directly to a laptop computer using custom designed software. Values for HR, MAP, SpO₂, and SctO₂ (and ECO₂ and BIS after induction of anaesthesia) were then measured continuously and recorded until the time of tracheal extubation. Reductions of ≥20% in MAP (definition of hypotension) or SctO₂ (definition of a CDE) were calculated using reference (baseline) values obtained before induction of anaesthesia.

Approximately 10 min after baseline data were collected, the patient was positioned in an 80–90° sitting position. The head was maintained in a neutral position to avoid impairment of venous drainage. The FORE-SIGHT monitor was positioned so that clinicians had access to SctO₂ data. A suggested protocol for treatment of CDEs was provided to clinicians: (i) increase systemic arterial pressure with phenylephrine (80 μg) and (ii) increase FIO₂ concentrations. The timing and number of phenylephrine treatments were recorded on the laptop computer.

Aldrete scores were recorded by post-anaesthesia care unit (PACU) nurses blinded to group assignment. Aldrete scores were assessed on arrival to the PACU and then every 15 min thereafter until discharge. The times required to meet PACU discharge criteria and to achieve actual PACU discharge were recorded. Postoperative pain was treated with hydromorphone (0.5 mg), which was titrated to achieve pain scores ≤3 on a 0–10 scale (0, no pain; 10, worst pain imaginable). Patients were carefully assessed for any episodes of nausea, vomiting, or both during the PACU admission. The requirements for treatment of nausea or vomiting were also noted.

Patient characteristics that were recorded included age, sex, height, weight, pre-existing medical conditions, and preoperative medications. Intraoperative anaesthetic management data that were assessed included duration of anaesthesia, administration of crystalloids, doses of opioids and rocuronium provided intraoperatively, and temperature at the conclusion of the anaesthetic. The number of episodes of CDEs was determined for each patient; an episode was defined as a 2 min time interval with a ≥20% decrease in SctO₂ from baseline values. The percentage of CDEs that occurred in association with concurrent hypotensive episodes was calculated. The number of episodes of CDEs using absolute SctO₂ thresholds of 60% and 55% was also determined.

**Statistical analysis**

In a previous study, the average SctO₂ values of ~67% were observed in patients undergoing BCP shoulder surgery with general anaesthesia and ventilation to an ECO₂ of 30–32 mm

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Fig 1 CONSORT trial flow diagram for the study of the effect of ventilation on cerebral oxygenation in patients undergoing surgery in the BCP.
Hg. We hypothesized that SctO₂ would be increased by 4–5% in the study group. Group sample sizes of 31 and 31 achieve 80% power to detect a difference of 4.5 between the null hypothesis that both group means are 67.1% and the alternative hypothesis that the mean of the study 40–42 group is 71.6%, with estimated group standard deviations (SDs) of 6.2 and 6.2 and with a significance level (α) of 0.05 using a two-sided two-sample t-test. Seventy patients were studied to ensure complete data collection.

Discrete data were compared using Fisher’s exact test (NCSS, Kaysville, UT, USA). The Miettinen and Nurminen score was used to calculate the 99% confidence intervals for differences in percentages. Ordinal data and non-normally distributed continuous data are presented as the median and range. These data were compared between the groups using the Mann–Whitney U-test and within the groups using Wilcoxon’s signed-ranks test (StatsDirect, Cheshire, UK). The median differences and their 99% confidence intervals were calculated.

Normally distributed continuous data are presented as mean and SD. These data were compared using the unpaired t-test (NCSS), except for the haemodynamic and other data measured repeatedly over time. The mean differences and their 99% confidence intervals were calculated.

Haemodynamic, tCO₂, SpO₂, end-tidal sevoflurane concentrations, BIS, and SctO₂ data (i.e. the data measured repeatedly over time) were compared within and between the groups using a two-factor analysis of variance (ANOVA) with repeated measures on one factor, with the Holm–Sidak method for pairwise multiple comparisons in post hoc analysis (SigmaPlot 11.0, Systat Software, Inc., San Jose, CA, USA). These data were only analysed through 60 min because data were available for all but eight patients through that time, after which the number of patients for whom data were available began dropping off such that data were unavailable for 26 of the 70 patients (37%) in the study by 70 min.

Because of the large number of comparisons being made, the criterion for rejection of the null hypothesis established a priori was a two-tailed P<0.01 to help minimize the chance of a type I error.

Results

The CONSORT trial flow diagram for the present study is presented in Figure 1. Cerebral oximetry data were collected on all 70 subjects. The two groups were similar in all preoperative patient characteristics, including age, sex, height, weight, baseline haemoglobin values, and preoperative medical conditions (including hypertension) and medications (data not presented) (Table 1). Intraoperative management characteristics of the control and study groups are presented in Table 2. There were no significant differences observed between groups in total anaesthesia time, use of intraoperative fentanyl and rocuronium, or crystalloid administration and blood loss. End-tidal sevoflurane concentrations did not differ between the groups (Fig. 2) and depth of anaesthesia was similar between the groups (no significant differences in BIS values, data not shown).

Significant differences in tCO₂ endpoints were achieved in the control and study groups, with most patients maintained within the tCO₂ goals established in the protocol throughout the intraoperative period (Fig. 3). HR did not change significantly from baseline measures within either group until 44–60 min from induction, and there were no statistically significant differences between the groups at any time (Fig. 4). MAP measurements decreased from baseline values at several measurement times during the surgery, but no significant intergroup differences were observed (Fig. 5). Peripheral arterial oxygen saturation (SpO₂) values also did not differ between the groups, with the exception of one measurement time (18 min). The number of patients requiring phenylephrine treatments, as well the total doses of phenylephrine, were similar between the groups (Table 3).

Cerebral oxygenation (SctO₂) data are presented in Figure 6 and Table 3. Baseline SctO₂ (78.4 (4.1%) vs 77.6 (4.1%)) did not differ between the control and study groups (P=0.383 by the unpaired t-test). The ANOVA post hoc analysis revealed that SctO₂ values in the study 40–42 group did not decrease over time. In contrast, SctO₂ measurements in the control 30–32 group were lower than baseline values from 10 min post-

Table 1  Patient characteristics. Data are mean (SD), median (range), or number of patients (%). Study 40–42, patients ventilated to an end-tidal carbon dioxide concentration of 40–42 mm Hg; Control 30–32, patients ventilated to an end-tidal carbon dioxide concentration of 30–32 mm Hg; haemoglobin, preoperative haemoglobin measurement; MI, myocardial infarction; CHF, congestive heart failure; PVD, peripheral vascular disease; drinking history, alcohol consumption >2 drinks day⁻¹.

<table>
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<td>0 (0%)</td>
<td>—</td>
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<td>Previous CHF</td>
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<td>0 (0%)</td>
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<tr>
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<td>2 (5.6%)</td>
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<td>Drinking history</td>
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<td>1 (2.8%)</td>
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induction until 60 min ($P<0.01$ across time). Furthermore, SctO$_2$ was significantly lower in the control 30–32 group than the study 40–42 group from 16 min post-induction until 60 min ($P<0.01$ across time). The incidence of CDEs, defined as a ≥20% decrease in SctO$_2$ from baseline values, was higher in the control 30–32 group (55.6%) than it was in the study 40–42 group (8.8%, $P<0.0001$). Furthermore, the median (range) number of CDE was greater in the control 30–32 group compared with the study 40–42 group ($P=0.0003$). A total of 198 separate CDE episodes (≥20% decrease in SctO$_2$ from baseline for 2 min interval) were observed in the study population as a whole; 134 of the 198 CDEs (67.7%) were recorded during a period of hypotension (≥20% decrease in MAP). Furthermore, the median number of CDEs that occurred in the presence of hypotension were significantly higher in the control 30–32 group than in the study 40–42 group from 16 min post-induction until 60 min ($P<0.0001$). Furthermore, the median number of CDEs that occurred in the presence of hypotension were significantly higher in the control 30–32 group compared with the study 40–42 group ($P=0.0003$).

Clinical recovery data are presented in Table 2. The times from tracheal extubation until PACU admission did not differ between the groups. Aldrete scores assessed in the PACU were also similar. Although the median times required to meet discharge criteria were less in the study 40–42 group (69 min) compared with the control 30–32 group (81.5 min), these differences did not reach statistical significance ($P=0.158$). The incidence of nausea was 33.3% in the control 30–32 group and 8.8% in the study 40–42 group ($P=0.019$) during the PACU admission. The incidence of vomiting was low in both groups and not significantly different.

**Discussion**

Appropriate intraoperative management of surgical patients in the BCP has been identified as an important patient safety issue. Altering mechanical ventilation in order to raise $\text{F}^{CO_2}$ values is a relatively simple method of potentially increasing CBF and SctO$_2$ values. However, relative changes in CBF during alterations in $\text{F}^{CO_2}$ can be influenced by baseline blood flow and pressure, which may be compromised in the BCP. In this clinical trial, significant reductions in SctO$_2$ measurements from baseline values were observed in patients ventilated to an $\text{F}^{CO_2}$ of 30–32 mm Hg, which occurred 10 min after induction of anaesthesia and persisted throughout the intraoperative period. In addition, a high incidence of CDEs (56%) was noted in this group. In contrast, SctO$_2$ values remained unchanged in the study 40–42 group and a lower incidence of CDEs (9%) was recorded in this group. Furthermore, a relationship between hyperventilation, hypotension, and CDEs was demonstrated, which suggests that ventilation to an $\text{F}^{CO_2}$ of 30–
32 mm Hg may compromise brain oxygenation in the setting of low arterial pressure.

Several clinical trials have assessed the incidence of CDE during shoulder surgery in the BCP. In an observational study of 124 patients undergoing the procedure in the BCP or lateral decubitus position under general anaesthesia, the percentage of patients with CDEs (≥ 20% decreases in SctO2 from baseline values) was significantly higher in the BCP cohort (80% vs none in the lateral decubitus group). An investigation using a similar study design also found decreases in SctO2 of >20% occurred in 80% of patients when the BCP was adopted. In contrast to these studies, fewer CDEs have been observed when BCP surgery is performed under regional anaesthesia. An observational study of 60 patients reported that CDE occurred in 57% of patients administered a general anaesthetic for BCP shoulder surgery, and in none undergoing the same procedure with an interscalene block and sedation. Similarly, only 10% of patients undergoing shoulder surgery in the sitting position with regional anaesthesia and sedation had >20% reductions in SctO2, despite the induction of hypotension in 76% of the observations.

There are several reasons why SctO2 is better maintained under regional anaesthesia in the sitting position. Significant reductions in arterial pressure and cardiac index occur when position is altered from supine to sitting in patients under general anaesthesia; these variables are minimally altered in the sedated patient during position change. Cardiac output may be further compromised by reductions in venous return during positive pressure ventilation. In addition, hyperventilation was used in patients receiving general anaesthesia, whereas mild hypoventilation was likely present in patients administered regional anaesthesia with sedation and spontaneous ventilation.

Many clinicians routinely adjust mechanical ventilation to achieve ECO2 values of 30–32 mm Hg intraoperatively. Several investigations have demonstrated that hyperventilation in surgical patients can reduce regional SctO2. In unshunted patients undergoing carotid endarterectomy surgery, altering the ECO2 from 40–45 to 30–35 mm Hg resulted in a 5–6% decrease in SctO2. In healthy elective surgical patients, ventilation adjustment from an ECO2 of 45 mm Hg to an ECO2 of 25 mm Hg resulted in a 4.3% decrease in SctO2. These findings are not unexpected. Arterial carbon dioxide is an important regulator of CBF, independent of autoregulation. The patient undergoing BCP surgery may be at particular risk for decreases in SctO2 with hyperventilation, as significant reductions in cerebral perfusion pressure and blood flow can occur after positioning. Because of the potential additive adverse effects of the sitting position and hyperventilation on CBF and oxygenation, it has been recommended that hyperventilation and low ECO2 be avoided in the BCP.
supine to sitting. A reduction in arterial pressure below an individual patient’s lower limit of autoregulation can result in cerebral ischaemia (detected with NIRS), and, if persistent, can produce stroke or coma. Furthermore, in the BCP, arterial pressure measured at the brachial artery may overestimate the actual pressure at the brain. Several case reports have described significant reductions in S\textsubscript{ctO2} after episodes of hypotension in the BCP.\textsuperscript{21, 22} In the present study, hypotension requiring treatment occurred frequently in the study population as a whole; 76% of patients required phenylephrine boluses to treat hypertensive episodes. There were no significant differences between the two groups in the incidence or treatments of hypertensive events. However, an association between hypotension (≥20% decrease in MAP from baseline) and CDEs (≥20% decrease in S\textsubscript{ctO2} from baseline) was observed. A majority of the CDEs (68%) were recorded during a period of hypotension, and the median number of CDEs that occurred during a hypertensive episode was significantly higher in the control 30–32 group. Our findings support previous observations that low intraoperative S\textsubscript{ctO2} is frequently associated with both hypotension and hyperventilation.\textsuperscript{16}

CDEs, defined as a ≥20% decrease in S\textsubscript{ctO2} from baseline value, were observed in 56% of the control 30–32 group and 9% of the study 40–42 group. At the present time, there is no universally accepted threshold S\textsubscript{ctO2} value that represents pathological cerebral ischaemia. This threshold value, and the incidence of CDEs, may be influenced by the NIRS technology used, the time of baseline measurement (post-induction S\textsubscript{ctO2} values are higher than preinduction S\textsubscript{ctO2} values), and patient factors (presence of cerebrovascular disease, age, haemoglobin levels).\textsuperscript{23, 24} Previous studies have demonstrated that decreases in S\textsubscript{ctO2} of 15–25% are associated with adverse events, which include fainting,\textsuperscript{25} symptoms of cerebral ischaemia in carotid endarterectomy patients,\textsuperscript{26} cognitive dysfunction after hip and cardiac surgery,\textsuperscript{27, 28} and longer PACU and hospital admissions after abdominal surgery.\textsuperscript{29} In the present study, no obvious permanent neurological events were identified in either group, despite the frequent observation of CDEs [although one patient in the control 30–32 group with a 34 min CDE (S\textsubscript{ctO2} 38–45%) exhibited transient delirium in the PACU]. These results are not surprising. Neurophysiological impairment is related to not only the severity of the CDE but also the duration of the event. In animal models, structural brain damage or selective neuronal death requires persistence of moderate reductions in S\textsubscript{ctO2} for at least 60–120 min.\textsuperscript{30} However, neurological injury may occur over a shorter period of time during severe reductions in S\textsubscript{ctO2} (e.g. during normothermic circulatory arrest). It is possible that CDEs of a shorter duration might result in more subtle cerebral injury. However, neurocognitive testing was not performed in this investigation.

Early recovery variables were similar between the groups. The times required to meet discharge criteria and achieve
actual PACU discharge were less in the study 40–42 group than the control 30–32 group, although they were not statistically significant. Nausea was observed during the PACU admission in 33% of patients in the control 30–32 group compared with 9% of those in the study 40–42 group. While the P-value for this difference was 0.019 (Table 2), it was not considered to be statistically significant because we had established the criterion for rejection of the null hypothesis a priori as a two-tailed P < 0.01 to help minimize the chance of a type I error. For this difference in proportions to have been statistically significant with 90% power and a two-tailed P < 0.01 as the criterion for rejection of the null hypothesis, the sample size in each group would have had to have been 83, more than twice what it was in the present study. Previously, a seven-fold higher incidence of nausea was noted in patients with intraoperative CDE during BCP surgery. Furthermore, in patients undergoing spinal anaesthesia, an association between hypotension, decreases in cerebral oxygenation, and nausea at the end of surgery has been reported. These findings suggest that reductions in cerebral perfusion and oxygenation during a surgical procedure may contribute to postoperative nausea and vomiting.

Some investigators have questioned the accuracy of NIRS technology in detecting cerebral ischaemia in the sitting position. All NIRS devices measure an uncertain mixture of arterial and venous blood, and SctO₂ values are calculated based on the assumption of a fixed arterial (25–30%)/venous (75–70%) ratio. Changes in position can potentially alter the ratio of the arterial to venous compartments in the cerebral circulation. However, minimal changes in SctO₂ are observed in patients undergoing BCP surgery with regional anaesthesia and sedation, which suggests this mechanism alone does not account for the observed high incidence of CDEs reported in previous studies.

Table 3 Primary outcome variables. Data are number of patients (%) or median (range). Ninety-nine per cent confidence intervals for the differences in percentages were calculated using the Miettinen and Nurminen score (NCSS). For a given variable, the difference between two medians and the 99% confidence interval for the difference were estimated from all possible differences between the two groups (StatsDirect). Study 40–42, patients ventilated to an end-tidal carbon dioxide concentration of 40–42 mm Hg; Control 30–32, patients ventilated to an end-tidal carbon dioxide concentration of 30–32 mm Hg; SctO₂, cerebral oxygenation (%); MAP, mean arterial pressure

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<th>Study 40–42 group</th>
<th>Control 30–32 group</th>
<th>Difference (99% CI)</th>
<th>P-value</th>
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<tr>
<td>Number</td>
<td>34</td>
<td>36</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Patients with cerebral desaturation events</td>
<td>3 (8.8%)</td>
<td>20 (55.6%)</td>
<td>−46.7% (−68.1% to −19.0%)</td>
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</tr>
<tr>
<td>Phenylephrine interventions for SctO₂ drops (n)</td>
<td>3 (0–36)</td>
<td>4 (0–19)</td>
<td>0 (−3 to 2)</td>
<td>0.794</td>
</tr>
<tr>
<td>Phenylephrine dose (μg)</td>
<td>240 (0–2.880)</td>
<td>320 (0–1.500)</td>
<td>0 (−240 to 160)</td>
<td>0.644</td>
</tr>
<tr>
<td>Episodes SctO₂ ≤ 55%</td>
<td>0 (0–1)</td>
<td>0 (0–18)</td>
<td>0 (0–0)</td>
<td>0.097</td>
</tr>
<tr>
<td>Events n</td>
<td>33</td>
<td>31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SctO₂ ≤ 60%</td>
<td>0 (0–8)</td>
<td>0 (0–18)</td>
<td>0 (−1 to 0)</td>
<td>0.0045</td>
</tr>
<tr>
<td>Episodes SctO₂ ≥ 20% decrease SctO₂</td>
<td>0 (0–21)</td>
<td>1 (0–30)</td>
<td>−1 (−3 to 0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Events n</td>
<td>31</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 20% decrease SctO₂ and MAP</td>
<td>0 (0–15)</td>
<td>0.5 (0–19)</td>
<td>0 (−3 to 0)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Events n</td>
<td>31</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2–4</td>
<td>1–3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>6–10</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>1</td>
<td>14–18</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>30</td>
<td></td>
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<tr>
<td></td>
<td>1</td>
<td>12–19</td>
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<td>15</td>
<td>6–8</td>
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<tr>
<td></td>
<td></td>
<td>12–19</td>
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</tr>
</tbody>
</table>
using jugular venous bulb oxygen saturation ($\text{SjO}_2$) and real-time electroencephalographic monitoring have demonstrated that reductions in cerebral oxygenation are not uncommon when surgery is conducted in the BCP with general anaesthesia.

There are limitations to the investigation. Direct measurement of $P_\text{ACO}_2$ was not performed. In healthy patients, $\text{ScCO}_2$ is a reliable estimate of $P_\text{ACO}_2$, and the change in $\text{ScCO}_2$ closely approximates the change in $P_\text{ACO}_2$. It is possible that the relationship between pulmonary blood flow and ventilation may be altered in the BCP, resulting in an increased gradient between $\text{ScCO}_2$ and $P_\text{ACO}_2$. Our study was designed to examine whether altering ventilation in healthy patients based on a routinely monitored endpoint ($\text{ScCO}_2$) could beneficially influence brain oxygenation. Secondly, clinicians providing intraoperative care were not blinded to $\text{ScCO}_2$ data, as our IRB stated that it would be unethical to withhold treatment of CDEs. This may have resulted in a significantly lower incidence and severity of cerebral desaturations in both study groups. Finally, our study was not powered to examine the effect of ventilatory management on clinical recovery. Our data suggest that some recovery variables may be improved when $\text{ScCO}_2$ values of 40–42 mm Hg are targeted, although larger clinical trials are needed.

In conclusion, our findings demonstrate that cerebral oxygenation is better maintained during BCP surgery when patients are ventilated to an $\text{ScCO}_2$ of 40–42 mm Hg compared with an $\text{ScCO}_2$ of 30–32 mm Hg. The majority of CDEs occurred when MAP was more than 20% below baseline values. Hypotension should be avoided when patients are undergoing BCP surgery with general anaesthesia, particularly in the setting of hyperventilation.

**Authors’ contributions**

G.S.M.: study design, data collection, data analysis, and manuscript preparation; J.W.S.: study design and manuscript preparation; M.J.A.: study design, data analysis, and manuscript preparation; S.B.G.: study design and manuscript preparation; T.D.S.: study design and manuscript preparation; J.S.V.: study design and manuscript preparation; S.D.L.: patient recruitment; J.L.K.: patient recruitment; K.N.P.: patient recruitment and study design; S.S.P.: patient recruitment and study design.

**Declaration of interest**

G.S.M. and S.B.G. have received speaker fees from CASMED.

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**References**

7. Drummond JC, Hargens AR, Patel PM. Hydrostatic gradient is important—blood pressure should be corrected. *APSF Newsletter* 2009; 24: 6

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**Fig 6** Regional cerebral oxygen saturation ($\text{ScO}_2$) for the patients in the control (end-tidal carbon dioxide = 30–32 mm Hg) group and in the study (end-tidal carbon dioxide = 40–42 mm Hg) group. The data are presented as mean (So). Time is minutes since induction of anaesthesia, with preinduction baseline measurements presented at time 0 min. The solid horizontal line indicates the time during which the $\text{ScO}_2$ s in the patients of the control group differed from their baseline $\text{ScO}_2$ s (10–60 min, overall $P<0.01$). The dashed horizontal line indicates the times during which the $\text{ScO}_2$ s in the patients of the study group differed from those in the control group (16–60 min, overall $P<0.01$). The numbers of patients in the control group and in the study group were 36 and 34, respectively, at baseline and decreased to 31 in both groups at 60 min.
Ventilation and cerebral desaturation events


17 Lee L. APSF workshop: cerebral perfusion experts share views on management of head-up cases. APSF Newsletter 2009; 24: 46–8


35 McSwain SD, Hamel DS, Smith PB, et al. End-tidal and arterial carbon dioxide measurements correlate across all levels of physiologic dead space. Respir Care 2010; 55: 288–93

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