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## SCIENTIFIC ARTICLE

# Impact of hypotension and global hypoperfusion in postoperative delirium: a pilot study in older adults undergoing open colon surgery



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### KEYWORDS

Delirium;  
Hypotension;  
Global perfusion;  
Central venous  
oxygen saturation;  
Lactate;  
Cerebral oxygenation

### Abstract

**Background:** Post-operative delirium is a serious complication in patients undergoing major abdominal surgery. It remains unclear whether peri-operative hemodynamic and perfusion variables affect the risk for postoperative delirium. The objective of this pilot study was to evaluate the association between perfusion and hemodynamics peri-operative with the appearance of post-operative delirium.

**Methods:** Prospective cohort study of adults 60 years or older undergoing elective open colon surgery. Multimodal hemodynamic and perfusion variables were monitored, including central venous oxygenation (ScvO<sub>2</sub>), lactate levels, and non-invasive cerebral oxygenation (rSO<sub>2</sub>), according to a standard anesthesia protocol. Fisher's exact test or Student's *t*-test were used to compare patients who developed post-operative delirium with those who did not ( $p < 0.05$ ). **Results:** We studied 28 patients, age  $73 \pm 7$  years, 60.7% female. Two patients developed post-operative delirium (7.1%). These two patients had fewer years of education than those without delirium ( $p = 0.031$ ). None of the peri-operative blood pressure variables were associated with incidence of post-operative delirium. In terms of perfusion parameters, postoperative ScvO<sub>2</sub> was lower in the delirium than the non-delirium group, without reaching statistical significance ( $65 \pm 10\%$  vs.  $74 \pm 5\%$ ;  $p = 0.08$ ), but the delta-ScvO<sub>2</sub> (the difference between means post-operative and intra-operative) was associated with post-operative delirium ( $p = 0.043$ ). Post-operative lactate and rSO<sub>2</sub> variables were not associated with delirium.

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**PALAVRAS-CHAVE**

Delírio;  
Hipotensão;  
Perfusão global;  
Saturação venosa  
central de oxigênio;  
Lactato;  
Oxigenação cerebral

**Conclusions:** Our pilot study suggests an association between delta ScvO<sub>2</sub> and post-operative delirium, and a tendency to lower post-operative ScvO<sub>2</sub> in patients who developed delirium. Further studies are necessary to elucidate this association.

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### Impacto da hipotensão e hipoperfusão global sobre o delírio pós-operatório: um estudo piloto com idosos submetidos à cirurgia aberta do cólon

**Resumo**

**Justificativa:** O delírio pós-operatório é uma complicação séria em pacientes submetidos à cirurgia abdominal de grande porte. Ainda não está claro se as variáveis hemodinâmicas e de perfusão no período perioperatório afetam o risco de delírio pós-operatório. O objetivo deste estudo piloto foi avaliar a associação entre perfusão e hemodinâmica no perioperatório com o surgimento de delírio pós-operatório.

**Métodos:** Estudo prospectivo de coorte de adultos com 60 anos ou mais de idade, submetidos à cirurgia eletiva aberta do cólon. As variáveis multimodais de hemodinâmica e perfusão foram monitoradas, incluindo oxigenação venosa central (ScvO<sub>2</sub>), níveis de lactato e oxigenação cerebral não invasiva (rSO<sub>2</sub>), de acordo com um protocolo padrão de anestesia. O teste exato de Fisher ou o teste-*t* de Student foram utilizados para comparar os pacientes que desenvolveram delírio pós-operatório com aqueles que não desenvolveram ( $p < 0,05$ ).

**Resultados:** Avaliamos 28 pacientes,  $73 \pm 7$  anos de idade, 60,7% do sexo feminino. Dois pacientes desenvolveram delírio pós-operatório (7,1%). Esses dois pacientes tinham menos anos de escolaridade que aqueles sem delírio pós-operatório ( $p = 0,031$ ). Nenhuma das variáveis de pressão arterial no perioperatório foi associada à incidência de delírio. Quanto aos parâmetros de perfusão, ScvO<sub>2</sub> foi menor no grupo que apresentou delírio pós-operatório que no grupo que não apresentou delírio, sem atingir significância estatística ( $65 \pm 10\%$  vs.  $74 \pm 5\%$ ;  $p = 0,08$ ), mas o delta-ScvO<sub>2</sub> (a diferença entre as médias no pós-operatório e intraoperatório) foi associado ao delírio ( $p = 0,043$ ). As variáveis de lactato e rSO<sub>2</sub> no pós-operatório não foram associadas ao delírio.

**Conclusões:** Nosso estudo piloto sugere uma associação entre delta-ScvO<sub>2</sub> e delírio e uma tendência à diminuição da ScvO<sub>2</sub> no pós-operatório de pacientes com delírio. Estudos adicionais são necessários para elucidar essa associação.

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**Introduction**

Post-operative delirium (POD) is an important complication in older adults undergoing major abdominal surgery.<sup>1</sup> POD is associated with increased morbidity, mortality, and long-term functional and cognitive impairment.<sup>2-4</sup>

The most commonly recognized risk factors for POD are old age, previous cognitive disorder, sensory impairment, severe illness, and infection.<sup>5,6</sup> Functional impairment, low education level, and alcohol abuse have also been suggested to increase risk. The impact of intra- and post-operative risk factors is controversial.<sup>7</sup> One element that has received considerable attention is intra-operative hypotension. While some authors have suggested an association between intra-operative hypotension and POD, other studies have failed to confirm the finding.<sup>8,9</sup>

During a major surgery, there is a risk of hemodynamic disturbance and brain or global hypoperfusion.

Pre-operative preparations, surgical bleeding, and the effects of anesthesia can increase the risk of real or relative hypovolemia, myocardial depression, and changes in vascular resistance that can trigger arterial hypotension and global or regional cerebral hypoperfusion, both during and after surgery. In addition, aging may reduce functional brain reserve and autoregulation of cerebral blood flow, making the organ more vulnerable to small hemodynamic changes.<sup>10,11</sup> Although there is a clear relationship between hemodynamic alteration and perfusion, few studies have systematically evaluated whether global or regional hypoperfusion are associated with POD. Therefore, we conducted a pilot study on a cohort of older adults undergoing open colorectal surgery, with the objective of evaluating whether peri-operative disturbances in hemodynamic parameters, global perfusion, and/or cerebral oxygenation are associated with POD. Our hypothesis was that global and cerebral hypoperfusion are associated with the development of POD.

## Methods

### Design

All patients who met eligibility criteria were consecutively enrolled in this prospective cohort study. Patients were subjected to multimodal hemodynamic, perfusion, and cerebral oxygenation monitoring, as well as standard anesthetic and surgical protocols, detailed below. Additional standardized information was collected from the medical records of enrolled patients.

### Ethical aspects

The study was approved by the Institutional Scientific Ethics Committee, and the patients gave their informed consent for participation.

### Patients

Consecutive patients aged 60 years or older, undergoing major open colon surgery for colon cancer, colostomy reversal, inflammatory bowel disease, diverticular disease, or megacolon, were enrolled and evaluated by the coloproctology team at our hospital. Exclusion criteria were: a) previous cognitive impairment, as indicated by a score of <22 on the version of the Mini-Mental State Examination (MMSE) instrument validated for our country<sup>12</sup>; b) indication for urgent or emergency surgery; or c) anticipated need for post-operative mechanical ventilation in the ICU.

### Baseline information

Pre-operative information on demographic variables and known risk factors for POD was obtained, including age, gender, years of education, functional status, comorbidities, and stratification of pre-operative anesthesia risk (ASA Physical Status Classification, American Society of Anesthesiologists). In addition, blood samples were collected to measure hemoglobin, creatinine, albumin, and lactate levels. Hemoglobin was measured with photometry using a hematology analyzer (ADVIA 2120, Siemens, Munich, Germany), and albumin, lactate, and creatinine were measured with colorimetric assay using a chemistry system (Vitros 5.1, Johnson & Johnson, New Jersey, US).

### Anesthesia protocol

After admission to the operating room, electrocardiographic (ECG) and continuous pulse oximetry (SpO<sub>2</sub>) monitoring were initiated. A catheter was then inserted into the radial artery for continuous monitoring of arterial pressure. These systems were connected to a CardiCap<sup>®</sup> 5 monitor (Datex Ohmeda<sup>®</sup>, GE Healthcare, Madison, WI, USA). After the baseline monitoring was initiated, an epidural catheter was inserted for post-operative analgesia. A sensor for monitoring depth of anesthesia was applied and connected to a Bispectral Index (BIS<sup>TM</sup>) monitor (Medtronic, Minneapolis, MN, USA). A non-invasive cerebral oximetry sensor

(rSO<sub>2</sub>) was then applied and connected to an INVOS 5100<sup>TM</sup> monitor (Medtronic, Minneapolis, MN, USA) according to manufacturer recommendations. In accordance with recommendations, baseline rSO<sub>2</sub> was recorded after a 1-min stabilization period with patients breathing 3 L·min<sup>-1</sup> O<sub>2</sub> by nasal cannula.

After the monitoring and anesthesia induction were initiated, a central venous catheter was inserted (Pre-Sep catheter, Edwards Lifesciences, Irvine, CA, USA). This catheter was subjected to *in vitro* calibration according to manufacturer instructions prior to insertion and connected to a Vigileo<sup>TM</sup> (Edwards Lifesciences) hemodynamic monitoring system for continuous monitoring of ScvO<sub>2</sub>.

Administration and monitoring of inhalation anesthesia were performed using an Aestiva 5 anesthesia machine (Datex Ohmeda<sup>®</sup>, GE Healthcare).

Anesthesia induction was performed with a propofol 2 mg·kg<sup>-1</sup> IV bolus, Target-Controlled Infusion (TCI) of remifentanyl, and cisatracurium 0.2 mg·kg<sup>-1</sup> IV bolus. In addition, patients were administered dexamethasone 4 mg IV, ondansetron 4 mg IV, ketoprofen 100 mg IV, and antibiotic prophylaxis with ceftriaxone 1 g IV plus metronidazole 500 mg IV. Hemodynamic parameters, ScvO<sub>2</sub>, BIS values, and NIRS values were recorded every 5 min during anesthesia. The rSO<sub>2</sub> and ScvO<sub>2</sub> measurements were masked to the attending anesthesiologist.

Anesthesia maintenance was performed using 1% isoflurane, targeting BIS values of 45–65, and TCI remifentanyl as needed.

Ventilation and fluid management were as follows: tidal volume of 6 mL·kg<sup>-1</sup> ideal weight, adjusting respiratory frequency to target EtCO<sub>2</sub> values of 30–35 mmHg, FiO<sub>2</sub> 0.5, and PEEP of 6 cm H<sub>2</sub>O. Lactated Ringer's solution 3–5 mL·kg<sup>-1</sup>·h<sup>-1</sup> was administered for fluid management, targeting a mean arterial pressure (MAP) of 65–85 mmHg. In the case of hypotension, variability of pulse pressure was monitored to evaluate for the need to administer an additional fluid bolus. In the case of severe hypotension or hypotension unresponsive to fluids, vasopressors were administered according to the following protocol: in the absence of tachycardia, a 6–12 mg bolus of ephedrine was administered; if there was no response to ephedrine or if ephedrine could not be used, a 50–100 µg bolus of phenylephrine was administered. If there was no response to phenylephrine, norepinephrine infusion was initiated, targeting a MAP of 65–85 mmHg.

Before the surgery was completed, epidural analgesia was initiated with a solution of 0.1% bupivacaine plus fentanyl 4 µg·mL<sup>-1</sup> at an infusion rate of 5–8 mL·h<sup>-1</sup>. Post-operative analgesia was performed by a specialized team from the Anesthesiology Department.

### Post-operative protocol

When the surgical procedure and anesthesia were complete, patients were transferred to the intermediate surgical unit of the Critical Care Unit, for continuous monitoring. Hemodynamic and perfusion parameters were recorded hourly, and arterial lactate and hemoglobin were measured every 6 h, until 24 h of monitoring had been completed.

## Delirium evaluation

Patients were evaluated daily for POD for 1 week, beginning on the day of surgery. The Confusion Assessment Method (CAM), an instrument validated for this condition, was used for this assessment.

## Definitions and cutoff points for variables of interest

As there is no standard definition of intra-operative hypotension, mean arterial, systolic, and diastolic pressure; minimum pressure; and variance in MAP were analyzed. The Area Under the Curve (AUC) was calculated for absolute minimum MAP values below 50 and 60 mmHg, as well as for intra- and post-operative values representing >20% and >30% decrease below baseline. For cerebral Near-Infrared Spectroscopy (NIRS), abnormal measurements were defined as: 1) 20% decrease in rSO<sub>2</sub> below baseline; 2) absolute rSO<sub>2</sub> below 50%.<sup>13</sup> ScvO<sub>2</sub> was considered a continuous variable. To evaluate the impact of intra- and post-operative ScvO<sub>2</sub>, we performed a post hoc analysis of delta-ScvO<sub>2</sub>, defined as the difference between mean intra- and post-operative ScvO<sub>2</sub>, looking for cutoff of 10%, 15% and 20%.

## Statistical analysis and sample size

We estimated that 20% of patients would develop POD.<sup>14</sup> We also estimated that the POD group would have post-operative ScvO<sub>2</sub> values at least 10% lower than those without POD and that the post-operative ScvO<sub>2</sub> of the group without POD would be approximately 75% ± 8%.<sup>15,16</sup> Given these parameters, for an alpha of 0.05 and a power of 80%, a sample of at least 25 patients was needed (OpenEpi version 3). Statistical analysis was performed using SPSS<sup>®</sup>

version 21.0 (SPSS<sup>®</sup> Inc., Chicago, IL, USA). Baseline patient characteristics and intra- and post-operative measurements were expressed as a proportion, mean ± SD, or median (p25–p75), according to the data distribution. The Kolmogorov–Smirnov test was used to evaluate the distribution of continuous variables. To explore the associations between baseline, intra-operative, and post-operative variables and POD, comparison of medians was used or Chi-squared test, Fisher's exact test, or Student's *t*-test for independent samples, as appropriate. A *p*-value <0.05 was used for all analyses.

## Results

Between January 2010 and March 2013, 28 patients were enrolled in the study. Patient demographic characteristics were age 73 ± 7 years, female 60.7%, and education 10 ± 4 years. Indications for surgery were colon cancer (82.1%), colostomy reversal (14.3%), or other (3.6%). Pre-operative anesthesia risk classifications were ASA I (35.7%), and ASA II (64.3%). Baseline blood values were hemoglobin 11 ± 2 g.dL<sup>-1</sup> and lactate 1.2 ± 0.3 mEq.L<sup>-1</sup>.

The observed incidence of POD was 7.1% (2 cases). Among baseline patient characteristics, lower education level was associated with POD (4.5 ± 0.7 vs. 11 ± 4 years for POD vs. non-POD groups, *p* = 0.031).

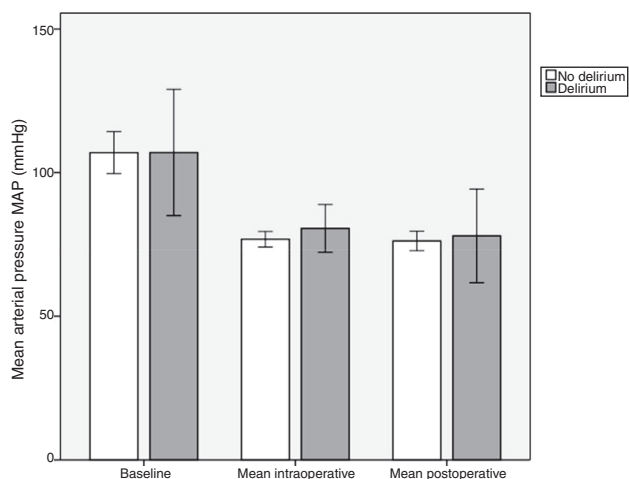
## Hemodynamic findings

Baseline parameters prior to anesthesia induction were mean arterial pressure (MAP) 107 ± 16 mmHg and Systolic Arterial Pressure (SAP) 157 ± 31 mmHg. All patients had at least one intra-operative episode of MAP below 65 mmHg, and 92.9% developed at least one episode of MAP below 60 mmHg. Intra-operative measurements for patients with and without delirium are presented in [Table 1](#).

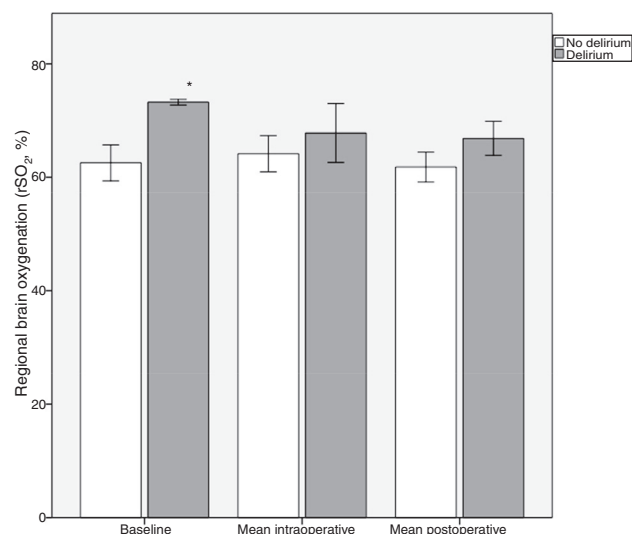
**Table 1** Absolute and relative intra-operative hemodynamics values for all patients, patients without post-operative delirium, and patients with post-operative delirium; data expressed as % and mean ± SD; *p*-values calculated using Student's *t*-test or Fisher's exact test.

	All patients (n = 28)	Patients without delirium (n = 26)	Patients with delirium (n = 2)	<i>p</i> -value
Baseline MAP (mmHg)	107 ± 16	107 ± 16	107 ± 16	0.997
Mean MAP (mmHg)	78 ± 6	76 ± 7	81 ± 6	0.473
Variance in MAP	250 ± 121	241 ± 123	342 ± 58	0.269
Lowest MAP (mmHg)	52 ± 4	52 ± 4	51 ± 4	0.654
Baseline SBP (mmHg)	157 ± 31	156 ± 32	160 ± 18	0.874
Mean SBP (mmHg)	114 ± 10	114 ± 10	114 ± 14	0.943
Variance in SBP	615 ± 318	597 ± 319	810 ± 326	0.378
Lowest SBP (mmHg)	73 ± 9	63 ± 4	74 ± 9	0.076
AUC MAP < 60 mmHg min	9 ± 48	89 ± 46	123 ± 81	0.353
AUC MAP < 50 mmHg min	4 ± 8	3 ± 8	10 ± 14	0.285
<b>Relative hypotension</b>				
20% decrease in MAP	60.7%	66%	100%	1.000
30% decrease in MAP	28.6%	40%	0%	0.515
40% decrease in MAP	7.1%	10%	0%	1.000
Mean HR	68 ± 12	67 ± 12	75 ± 21	0.449

MAP, mean arterial pressure; SBP, systolic pressure blood; AUC, area under the curve; HR, heart rate.



**Figure 1** Baseline, intra-operative, and post-operative mean arterial pressure (MAP, mmHg) in patients without and with delirium (mean ± 2 standard errors; n = 28 cases).



**Figure 2** Baseline, intra-operative, and post-operative cerebral oxygen saturation (rSO<sub>2</sub>, %) in patients without and with delirium (mean ± 2 standard errors; n = 28 cases).

Post-operative MAP was 76 ± 8 mmHg. Baseline, intra-operative, and post-operative MAP for patients with and without POD are shown in Fig. 1. There were significant differences between baseline vs. intra- and post-operative MAP (*p* < 0.001), but no significant differences between POD and non-POD groups.

Intra-operative fluids and vasopressor administration is described in Table 2. None of these variables were associated with the incidence of POD.

### Cerebral oxygenation

Mean baseline rSO<sub>2</sub> was 64% ± 7%. The evolution of baseline, intra-operative, and post-operative cerebral oxygen saturation measurements are shown in Table 3 and Fig. 2. There was a significant difference between patients with and without POD for baseline rSO<sub>2</sub> (*p* = 0.038) but not intra- or post-operative rSO<sub>2</sub>.

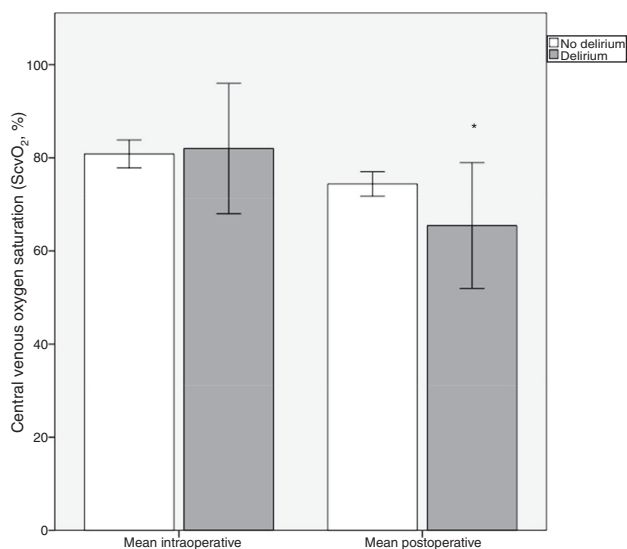
**Table 2** Intra-operative hemodynamic interventions and incidence of post-operative delirium.

	All patients (n = 28)	Patients without delirium (n = 26)	Patients with delirium (n = 2)	p-value
Fluids (mL)	1911 ± 985	1923 ± 1020	1750 ± 354	0.816
Ephedrine (%)	86%	85%	100%	1.000
Ephedrine dosage	38 ± 27	39 ± 28	30 ± 17	0.663
Phenylephrine (%)	57%	54%	100%	0.492
Phenylephrine dosage	493 ± 1172	470 ± 1216	775 ± 35	0.731
Norepinephrine (%)	25%	23%	50%	0.444
Surgery time	157 ± 62	161 ± 62	102 ± 17	0.197
Anesthesia time	216 ± 64	219 ± 65	177 ± 33	0.382

**Table 3** Intra- and post-operative characteristics of non-invasive brain oxygenation (rSO<sub>2</sub>, %) in all patients, patients without post-operative delirium, and patients with post-operative delirium (rSO<sub>2</sub>iop, intra-operative measurement; rSO<sub>2</sub>pop, post-operative measurement); data expressed as % and mean ± SD; p-values calculated using Student's *t*-test or Fisher's exact test.

	All patients (n = 28)	Patients without delirium (n = 26)	Patients with delirium (n = 2)	p-value
rSO <sub>2</sub> iop < 20% of baseline	43% (12/28)	38% (10/26)	100% (2/2)	0.175
rSO <sub>2</sub> iop < 50% (absolute value)	39% (11/28)	42% (11/26)	0% (0/2)	0.505
AUC rSO <sub>2</sub> iop < 20% of baseline	4.2 ± 8.6	4.3 ± 9	2.5 ± 1.0	0.776
AUC rSO <sub>2</sub> iop < 50% (absolute value)	7.6 ± 15	8.2 ± 16	0	0.478
rSO <sub>2</sub> pop < 20% of baseline	29% (8/28)	27% (7/26)	50% (1/2)	0.497
AUC rSO <sub>2</sub> pop < 20% (absolute value)	1.6 ± 3.7	1.7 ± 3.9	1.0 ± 1.3	0.791

AUC, area under the curve.



**Figure 3** Mean intra-operative and post-operative central venous oxygen saturation (ScvO<sub>2</sub>, %) in patients without and with delirium (mean ± 2 standard errors,  $n=28$  cases; \* $p=0.081$ ).

### Global perfusion parameters

There was a significant difference between intra- ( $81\% \pm 8\%$ ) and post-operative ( $74\% \pm 7\%$ ) ScvO<sub>2</sub> ( $p=0.003$ ). The mean intra-operative and post-operative ScvO<sub>2</sub> values for patients with and without delirium are presented in Fig. 3. Post-operative ScvO<sub>2</sub> was  $65\% \pm 10\%$  in the POD group vs.  $74\% \pm 7\%$  in the non-POD group ( $p=0.08$ ). In terms of delta ScvO<sub>2</sub>, patients with change  $>15\%$  had significantly higher incidence of POD than those with a lower delta ScvO<sub>2</sub> (Fisher's exact test,  $p=0.043$ ).

In terms of lactate measurements, 61% of patients had at least one lactate value above the normal limit. The mean maximum lactate value was  $2.7 \pm 1.6$  mEq.L<sup>-1</sup>, and in 25% of patients, the lactate peak was  $>4$  mEq.L<sup>-1</sup>. There was no association between lactate measures and POD.

### Discussion

Our pilot study evaluated the association between peri-operative hypotension, hypoperfusion and cerebral oxygenation and post-operative delirium in a population of elderly patients undergoing major abdominal surgery.

This pilot study was negative for the primary outcome; while post-operative ScvO<sub>2</sub> was lower among patients with vs. without POD, the difference was not significant ( $65\%$  vs.  $74\%$ ,  $p=0.08$ ). However, the delta-ScvO<sub>2</sub> was associated with the development of delirium. In terms of secondary outcomes, there was no association between peri-operative hypotension, decreased cerebral oxygenation, or hyperlactatemia with delirium. Additionally, we found that the years of education were associated with the occurrence of POD.

In relation to the global hypoperfusion markers, both the reduction in ScvO<sub>2</sub> and the increase in postoperative lactate have been associated with worse outcomes in surgical patients.<sup>15,16</sup> Moreover, it has been suggested that resuscitation strategies could impact peri-operative

morbidity and length of hospital stay, although these findings remain controversial.<sup>17,18</sup> Our study is the first to evaluate them in the onset of delirium. Our findings, although negative for the primary outcome, are provocative since the difference observed in postoperative ScvO<sub>2</sub> was 9% lower for patients that developed delirium, which seems clinically relevant for a pilot study. A high proportion of the patients developed hyperlactatemia, however, it was not associated with POD.

The association between intra-operative hypotension and delirium is controversial.<sup>8,9</sup> Some studies suggest an association; however, recent publications employing new strategies for analysis of intra-operative hypotension have not confirmed this finding. Our study, consistent with those recent studies, found no association between hypotension and delirium.

Regarding the relationship between cerebral oxygenation and delirium, several studies have associated reductions in non-invasive brain oxygenation and cognitive outcomes, particularly in cardio-surgical patients.<sup>19,20</sup> In delirium, one study shows association between baseline rSO<sub>2</sub> and risk of delirium.<sup>13</sup> Our findings did not confirm this observation.

Finally, we observed an association between years of education and POD. This finding has been reported previously, although this variable is overlooked in many studies. This finding speaks to the relevance of cognitive reserve as a critical factor in baseline POD risk. This concept is related to the pre-operative cognitive trajectory, which has recently been suggested as a critical variable in the risk for post-operative neurological complications.<sup>21,22</sup>

The primary limitation of this study is its small sample size. Given the multiplicity of pre-operative and intra-operative variables linked to POD, we designed a strict protocol with a group of very homogeneous patients. Our study followed a standardized protocol for anesthetic and surgical procedures, including monitoring and management of hemodynamic disturbances and depth of anesthesia.

Another limitation, not expected a priori, was the low observed incidence of POD, which was at the lower limit described in the literature for this type of patient. This finding may be attributable to the protocol's positive effects on clinical practices. Although not planned, it is possible that the protocol finds impacted other practices such as the use of benzodiazepines, or other drugs that may be associated to the development of delirium. Other potential source is the depth-of-anesthesia monitoring strategies used. Several studies have suggested that monitoring depth of anesthesia with BIS reduces risk of delirium.<sup>23,24</sup> Because these effects may have led to an underpowered study, the findings from this pilot study should be treated as hypothesis generators, particularly the relationship between peri-operative ScvO<sub>2</sub> and delirium.

Despite the limitations described, it seems to us that its design and interesting findings may provide some future perspectives in relation to the study in this area. First, among the markers evaluated, the finding obtained with ScvO<sub>2</sub> seems the most promising. Future studies of global perfusion and POD should consider intra and post-operative measurement of ScvO<sub>2</sub> as well as their relationships. Second, it is advisable that future studies focus on populations at higher risk for POD. For this, different preoperative variables should be considered, allowing a better risk stratification.

Finally, new studies should consider sample size that allows to resolve the existence or not of association between cerebral hypoperfusion and delirium.

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## Conflicts of interest

The authors declare no conflicts of interest.

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