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Cerebral haemodynamic physiology during steep Trendelenburg position and CO₂ pneumoperitoneum

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Editor's key points

- Prolonged steep Trendelenburg, along with pneumoperitoneum, may influence cerebral perfusion.
- Zero flow pressure (ZFP) is the theoretical pressure at which cerebral circulation ceases.
- ZFP was calculated in 14 patients undergoing prolonged Trendelenburg and pneumoperitoneum.
- Cerebral perfusion did not appear to be compromised and ZFP was a suitable measure in this setting.

Background. The steep (40°) Trendelenburg position optimizes surgical exposure during robotic prostatectomy. The goal of the current study was to elucidate the influence of this patient positioning on cerebral blood flow and zero flow pressure (ZFP), and to assess the validity of different methods of evaluating ZFP.

Methods. In 21 consecutive patients who underwent robotic endoscopic radical prostatectomy under general anaesthesia, transcranial Doppler flow velocity waveforms and invasive arterial and central venous pressure (CVP) waveforms suitable for analysis were recorded throughout the whole operative procedure in 14. The ZFP was determined by regression analysis of the pressure-flow plot and by different simplified formulas. The effective cerebral perfusion pressure (eCPP), pulsatility index (PI), and resistance index (RI) were determined.

Results. While patients were in the Trendelenburg position, the ZFP increased in parallel with the CVP. The PI, RI, gradient between the ZFP and CVP, and the gradient between the CPP and the eCPP did not increase significantly ($P < 0.05$) after 3 h of the steep Trendelenburg position. Using the formula described by Czosnyka and colleagues, the ZFP correlated closely with that calculated by linear regression throughout the course of the operation.

Conclusions. Prolonged steep Trendelenburg positioning and CO₂ pneumoperitoneum does not compromise cerebral perfusion. ZFP and eCPP are reliable variables for assessing brain perfusion during prolonged steep Trendelenburg positioning.

Keywords: arteries, cerebral; brain, intracranial pressure; measurement techniques, flow velocity waveform analysis, cerebral blood flow; surgery, urological

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Robotic endoscopic abdominal surgery requires a steep (40°) Trendelenburg positioning of the patient for several hours, along with a CO₂ pneumoperitoneum.^{1, 2} While this position offers significant surgical and technical advantages, it has the potential to significantly influence cerebral haemodynamic homeostasis. The patient population requiring robotic surgery are very vulnerable to perturbations in cerebral homeostasis, since they commonly also have problems that impair cerebral autoregulation, such as systemic hypertension and cerebrovascular disease. Thus, it is important to understand and quantify the influence of steep Trendelenburg positioning and pneumoperitoneum on cerebral homeostasis in this patient group.

The cerebral perfusion pressure (CPP), the driving pressure for brain perfusion, is usually regarded as the difference

between the mean arterial pressure (MAP) and the greater of the intracranial pressure (ICP) and the central venous pressure (CVP).³ In patients with normal physiology and under standard conditions, the equation $CPP = MAP - CVP$ provides a reasonable approximation of effective CPP (eCPP). If, however, significant cerebral perivascular oedema develops, it is conceivable that the eCPP deviates significantly from this theoretical value. Consequently, a CPP that is associated with adequate cerebral perfusion in the supine position may become inadequate after a long period of the steep Trendelenburg position. Decreasing eCPP caused by worsening perivascular oedema should be reflected in the evolution of the zero flow pressure (ZFP), which is the arterial pressure (AP) at which, theoretically, blood flow in the cerebral circulation ceases, and may represent the effective downstream

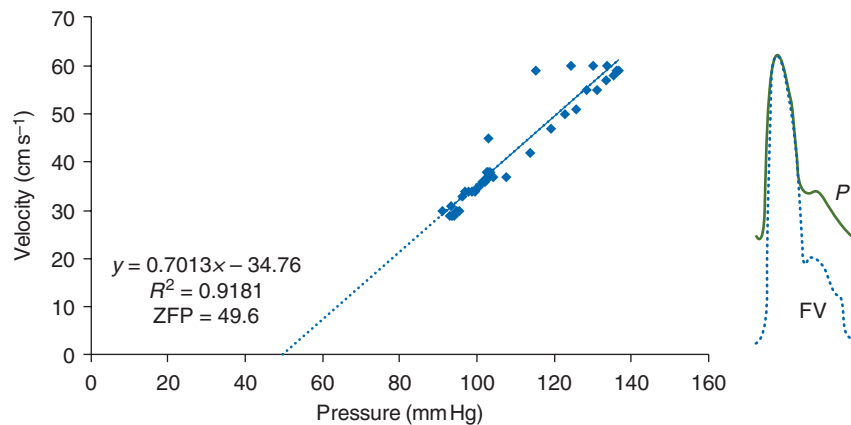


Fig 1 Determination of the ZFP by regression analysis of the pressure–flow plot of the flow velocity (FV) and invasive AP (P). Each dot of the flow velocity waveform represents a pressure sample and corresponds to a data point in the regression analysis. The X-intercept of the regression line is the ZFP. An $R^2 > 0.91$ is used as a cut-off value to select heartbeats with adequate signal quality.

pressure of this system.⁴ The evolution of the eCPP and ZFP can be estimated from analysis of the middle cerebral blood flow velocity (using Transcranial Doppler Sonography, TCD) and invasive AP waveforms. A clinically significant increase in the effective downstream pressure is likely to be reflected in a significant increase in the ZFP. Therefore, ZFP is a unique measure that can be used to assess the evolution of the vascular resistance to blood flow during surgery.

There are essentially two major methods for determining the ZFP. The most fundamental method calculates the ZFP by regression analysis of the pressure–flow plot (Fig. 1). This method is the most precise, but requires elaborate computations and perfect synchronization of the pressure and flow curves. The second general method uses a formula to calculate ZFP from the systolic and diastolic pressure and flow values⁵ (Fig. 2). The basic principle is that, mathematically, perfusion pressure = flow \times resistance. The two most commonly used formulas are those suggested by Czosnyka and colleagues⁶ and Schmidt and colleagues.⁷ These methods are much simpler to implement than regression analysis and can be used relatively easily for bedside assessments. As far as we are aware, neither the general method nor the different available formulae for calculating ZFP have been validated in patients in the extreme Trendelenburg position.

The main aim of this study was therefore to assess the influence of the extreme Trendelenburg positioning combined with CO₂ pneumoperitoneum on ZFP and eCPP over time. Here, our objective was to determine whether these factors cause a clinically significant increase in downstream pressure and cerebral vascular resistance. Our secondary aims were to assess the influence of this position, and changes in PaCO₂, on the pulsatility index (PI),⁸ resistance index (RI),⁹ and ZFP. Finally, we wished to evaluate the validity of the more practical formula-based methods for bedside determination of the ZFP in this position.

$$eCPP_{\text{Belfort}} = FV_m \times \frac{BP_m - BP_d}{FV_m - FV_d}$$

$$ZFP_{\text{Czosnyka}} = BP_s - FV_s \times \frac{BP_s - BP_d}{FV_s - FV_d}$$

$$ZFP_{\text{Schmidt}} = BP_m - \left(BP_m \times \frac{FV_d}{FV_m} + 14 \right)$$

$$RI = \frac{FV_s - FV_d}{FV_s}$$

$$PI = \frac{FV_s - FV_d}{FV_m}$$

Fig 2 Formulae to determine the eCPP as described by Belfort and colleagues,¹⁵ the ZFP as described by Czosnyka and colleagues⁶ and Schmidt and colleagues,⁷ and the RI and PI. All formulae are a function of the mean (m), diastolic (d), or systolic (s) value of the flow velocity (FV) and invasive AP.

Methods

After Institutional Ethics' Committee approval (Ethics' Committee, OLV Clinic, Aalst, Belgium) and written informed consent was obtained, 21 consecutive patients who underwent robotic endoscopic prostatectomy in the steep Trendelenburg position were included as a subset from a previously published study population.¹⁰

No premedication was given. Upon arrival in the operating theatre, standard monitoring was applied: ECG, pulse oximetry, and non-invasive automated AP. After anaesthesia was induced with propofol 1–2 mg kg⁻¹ and sufentanil 0.25 μ g kg⁻¹, rocuronium 0.6 mg kg⁻¹ was given and the trachea intubated. Anaesthesia was maintained with 1 MAC of sevoflurane. Additional boluses of sufentanil and

rocuronium were administered as required at the discretion of the clinician. The lungs were ventilated in a volume control mode with an O₂/air mixture (F_IO₂ 40%) and a PEEP of 5 cm H₂O. The tidal volume was adjusted to achieve a P_{E'}CO₂ between 4.0 and 4.7 kPa. Normothermia was maintained with a forced-air warming system. Once stable profiles of capnography and AP were reached, ventilatory and drug delivery settings were left unchanged.

After induction of anaesthesia, a 20 G arterial catheter (Arterial Cannula, REF 682245, Becton Dickinson, Swindon, UK) was inserted percutaneously into a radial artery. The catheter was connected via a rigid pressure tubing (length 150 cm, internal diameter 1.5 mm), filled with saline, to a continuous-flush pressure-transducer system (Becton Dickinson Critical Care Systems, Singapore) to monitor beat-to-beat AP. The right internal jugular vein was cannulated with a double-lumen central venous catheter (Arrow International Inc., Reading, PA, USA) for monitoring of CVP. The external acoustic meatus was used as the zero reference point for both pressure transducers, to allow a precise determination of the cerebral perfusion pressure, independent of patient positioning. Both systems were calibrated against atmospheric pressure and both pressure transducers were connected to an S5-monitor (GE Healthcare, Helsinki, Finland).

A middle cerebral artery was detected via the temporal window using a 2 MHz Transcranial Doppler ultrasound probe (dopbox, MedCaT, Erica, The Netherlands). The identity of the middle cerebral artery was confirmed using standard criteria¹¹ and the position of the probe was fixed with the DiaMon® Sets (Compumedics, Singen, Germany) monitoring set to maintain a constant angle of insonation. All waveforms were recorded on a personal computer. The waveform sampling frequency was 100 Hz.

After adequate positioning¹⁰ of the patient, the abdominal cavity was insufflated with CO₂ to a pressure of 10 mm Hg, and the patient was placed in the mild Trendelenburg position after which the trocars were located.¹² Finally, the patients were slowly placed in the steep Trendelenburg position (40° from horizontal). All operations were performed on the same table with the same degree of Trendelenburg.

The surgeon performed the procedure with the da Vinci Robot Surgical System (Intuitive Surgical, Sunnyvale, CA, USA). The intraperitoneal pressure was adjusted by the surgeon as needed. At the end of the procedure, the position of the table was normalized and the pneumoperitoneum was released. The surgical wounds were closed and the patient was awakened either in the operating theatre or in the recovery room. The patients were discharged to the ward after evaluation of the cognitive functions using Aldrete's score,¹³ based on AP, consciousness, O₂ saturation, respiratory rate, and recovery of motor functions.

Data analysis

All vital signs were monitored using an S5-monitor with automated electronic data recording using Collect Software (GE Healthcare). The AP and CVP waveforms were sampled and digitized at 100 Hz. All other variables were recorded digitally

every 5 s. In the subsequent offline analysis, the data, which were stored in the ASCII format, were imported into Microsoft Excel spreadsheets. Using dedicated custom-developed software (written by A.F.K.), the pressure waveforms were synchronized with the velocity waveforms for visual inspection and analysis.

Pressure and velocity waveforms of each individual heart beat over the whole operation were evaluated for perfect synchronization. Hysteresis in the pressure-flow velocity plots was minimized (for each heartbeat, the point of maximal positive slope of both waveforms was automatically synchronized) and the ZFP was calculated for every heart cycle as extrapolated by regression analysis of the pressure-flow plot¹⁴ (Fig. 1). These data are presented as ZFP_{reg}. As signal quality is of critical importance for reliable determination of derived values from pressure and flow variables, we only analysed those waveforms where the R² of the regression line was >0.91 (Fig. 1).

In those heartbeats with R²>0.91, the effective eCPP was calculated using the formula of Belfort and colleagues,¹⁵ the ZFP using the formulas described by Czosnyka and colleagues⁶ and Schmidt and colleagues,⁷ the RI⁹ as described by Pourcelet, and the PI⁸ as described by Gosling and King (Fig. 2).

The MAP and CVP were determined for each heartbeat (as the arithmetic mean of sampling values within each heartbeat) and the CPP was calculated as the difference between MAP and CVP.

These calculated values were determined at 10 min intervals from 5 min before institution of the Trendelenburg position to 30 min after resuming the supine position. For each interval, the mean (SD) was calculated for the values within a time window of 30 s (=6 ventilation cycles).

All curves were first synchronized with the onset of Trendelenburg positioning (T₀), and then later re-synchronized upon resumption of the supine position (represented as S in Fig. 3). The baseline value, reported as 'Pre', was defined as the average of the 30 s interval at 5 min before steep Trendelenburg repositioning (i.e. after induction of anaesthesia, during the period when the patient was still in the horizontal position, just before shallow Trendelenburg).

The relationship between the ZFP and the P_{E'}CO₂ after institution of the Trendelenburg position was determined by linear regression analysis (Fig. 4). For every 10 min period that each patient was in the Trendelenburg position, we determined the median of the ZFP and P_{E'}CO₂ values during the last 30 s of that period. The resulting data couples for all patients were then entered in the regression analysis.

Statistical analysis

Data were analysed using the two-sided Student *t*-test for paired comparisons and statistical significance level was set at 5%. Data were analysed using Excel 2007.

Results

Twenty-one patients were enrolled in the study. In four patients, no reliable TCD signal could be obtained at baseline,

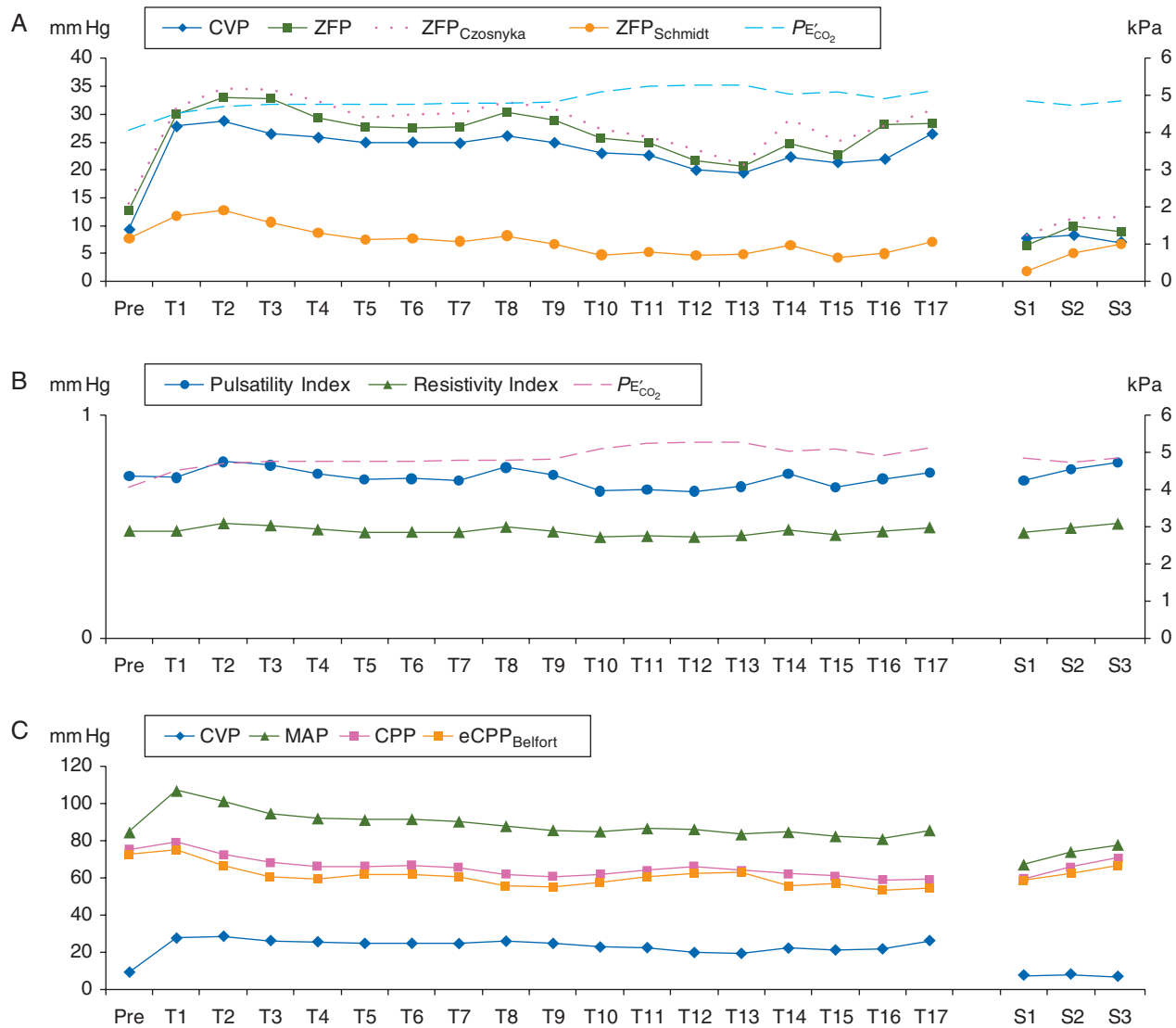


Fig 3 (A) CVP, ZFP calculated by linear regression (ZFP), ZFP as described by Czosnyka and colleagues⁶ and Schmidt and colleagues,⁷ and the end-tidal CO₂ pressure (P_{E_{CO₂}). (B) PI, RI, and P_{E_{CO₂}. (C) The course of the CVP, invasive MAP, CPP determined as (CPP=MAP–CVP), and the eCPP as described by Belfort and colleagues (eCPP_{Belfort}).¹⁵ The variables are shown as mean values at 10 min intervals. Pre-values are defined as the average of the 30 s interval at 5 min before steep Trendelenburg repositioning, after induction of anaesthesia. All data are synchronized at the moment of initiating Trendelenburg positioning and resynchronized at resumption of the supine position. The variables are shown as mean values at 10 min intervals from 5 min before to 165 min after institution of the Trendelenburg position. At reassuming the supine position, the curves are resynchronized and values are shown for another 20 min.}}

while in a further three patients, adequate signals were not obtainable in the Trendelenburg position. Data of the remaining 14 patients were normally distributed and are presented as mean (SD). The age of the patients was 63 (8) yr. The total time spent in the steep Trendelenburg position was 149 (83) min. All patients left the post-anaesthesia care with an Aldrete¹³ score of 10/10 and were discharged from hospital after an uneventful postoperative period.

CVP and ZFP calculated using linear regression and the Czosnyka formula, but not the Schmidt formula, increased in the Trendelenburg position (Table 1). MAP, CPP, and eCPP were lower in the post-Trendelenburg phase (Table 1). CVP

and ZFP_{reg} increased significantly after T₀. The gradient between these variables remained stable—mean ZFP_{reg} was 2.8 (8.6) mm Hg, greater than CVP during Trendelenburg positioning (P>0.05). Neither variable changed significantly during the period of Trendelenburg positioning (Fig. 3A).

The ZFP_{Czosnyka} increased significantly after T₀ and correlated closely with ZFP_{reg} (Fig. 3A). After resumption of the supine position, it was not significantly different from the value before Trendelenburg. The ZFP_{Schmidt} did not change significantly after T₀ and showed poor correlation with the ZFP (Fig. 3A).

Over the course of the operation, eCPP values were consistently lower than the calculated CPP (=MAP–CVP),

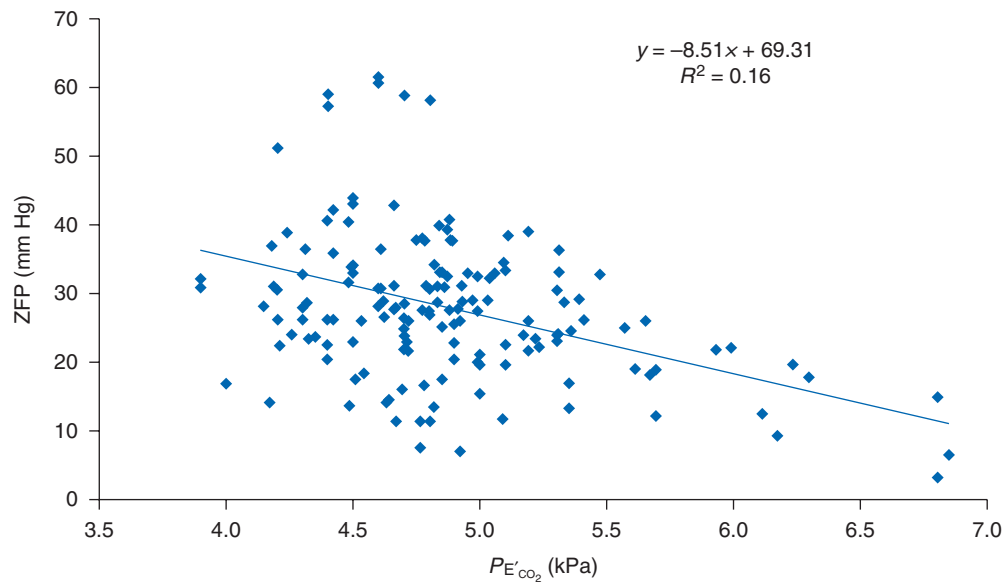


Fig 4 Linear regression analysis of the ZFP as a function of the PE'_{CO_2} .

Table 1 The perioperative changes in invasive MAP and CVP, measured at the level of the mid-ear, CPP calculated as $CPP = MAP - CVP$, effective CPP as described by Belfort, ZFP calculated by linear regression and as described by Czosnyka and Schmidt, end-tidal CO_2 pressure (PE'_{CO_2}), PI and RI of the patients in the period before (Pre-Tren), during (Tren), and after (Post-Tren) institution of the steep Trendelenburg position. Pre-Tren values are defined as the average of the 30 s interval at 5 min before steep Trendelenburg repositioning, but always after induction of anaesthesia. The values are shown as mean (sd) of the 14 patients included in the study. *Significantly different from the pre-Trendelenburg period, $P < 0.05$

	Pre-Tren	Tren	Post-Tren
MAP (mm Hg)	85 (12)	91 (11)	73 (14)*
CVP (mm Hg)	9 (5)	25 (8)*	8 (4)
CPP (mm Hg)	76 (12)	67 (13)	63 (14)*
eCPP _{Belfort} (mm Hg)	73 (15)	61 (10)	61 (20)*
ZFP _{linear regression} (mm Hg)	13 (7)	28 (11)*	8 (15)
ZFP _{Czosnyka} (mm Hg)	14 (8)	30 (11)*	10 (14)
ZFP _{Schmidt} (mm Hg)	8 (7)	8 (5)	4 (6)
PE'_{CO_2} (kPa)	4.1 (0.3)	4.9 (0.5)*	4.8 (0.6)*
Pulsatility index	0.73 (0.20)	0.72 (0.17)	0.75 (0.19)
Resistance index	0.48 (0.09)	0.48 (0.07)	0.49 (0.08)

although this difference did not reach statistical significance. Moreover, the gradient between the CPP and the eCPP did not increase significantly over the course of the operation (Fig. 3c).

The PI and RI did not change significantly over the course of the operation (Fig. 3b). The PE'_{CO_2} increased significantly

during the Trendelenburg position, compared with baseline (Fig. 3b). There is a tendency for the ZFP to decrease with increasing PE'_{CO_2} (Fig. 4). The negative slope confirms that the CO_2 reactivity of CBF is preserved and that a higher PE'_{CO_2} results in a safer AP threshold for brain perfusion.

Discussion

In this observational study of a group of 14 patients undergoing robotic prostatectomy, we have evaluated the influence of the steep Trendelenburg position combined with a CO_2 pneumoperitoneum on cerebral haemodynamic homeostasis. The steep Trendelenburg position (40°) optimizes surgical exposure and is advantageous in several procedures. However, the unphysiological positioning combined with the need for CO_2 pneumoperitoneum raises major concerns for the physiological homeostasis of the patient, especially for ICP and brain perfusion, although it seems to be well tolerated by most patients.¹⁰

The head-down position increases AP, but at the same time increases CVP, thus impairing venous outflow from the brain, and increasing hydrostatic pressures within the brain vasculature. As microvascular fluid exchange is governed by the balance between hydrostatic pressure and osmotic pressure, increasing the hydrostatic pressure will change the balance of these Starling forces.¹⁶ This is likely to increase the extracellular water content in dependent tissues. In the brain, this could eventually induce an increase in ICP and cerebral oedema, resulting in increased cerebrovascular resistance and reduced CBF. This combination of problems can cause impaired tissue oxygenation as a result of impaired perfusion and diffusion.

Other factors associated with this position will tend to increase CBF. As the increase in AP is greater than that in the CVP,¹⁰ the cerebral perfusion pressure (CPP) is increased. In the face of stable P_{aCO_2} levels, autoregulatory mechanisms would maintain constant CBF by vasoconstriction. In the clinical setting however, CO_2 levels are seldom stable and normal. Pneumoperitoneum may induce hypercarbia by impairing diaphragmatic excursion and minute volume of ventilation, and by systemic CO_2 absorption. The resulting cerebral vasodilation is likely to increase CBF. The overall impact of these opposing influences makes it difficult to predict the final impact of this positioning on the cerebrovascular resistance and cerebral blood flow.

An important variable to assess negative effects of possible cerebral oedema is the evolution of the ZFP. If cerebral oedema significantly increases the vascular resistance, this should be reflected in the ZFP. ZFP is determined by two Starling resistors in series, one at the pre-capillary arteriolar level influenced by vascular tone and the other at the level of collapsible cerebral veins influenced by the greater of the ICP and CVP.¹⁷ A Starling resistor is any collapsible conduit surrounded in its middle section by an external pressure that is greater than the outlet pressure.³ The pre-capillary Starling resistor determines the effective downstream pressure as long as the ICP (CVP) does not exceed the critical closing pressure of the arteriolar system. It remains to be seen whether the resistance of the second Starling resistor (at the level of the cerebral veins) remains at an acceptable level in the context of prolonged steep Trendelenburg position. ZFP of the cerebral circulation can be reasonably assessed from instantaneous pressure-flow velocity plots by extrapolation.¹⁷ This ZFP should be slightly higher than the CVP. If prolonged steep Trendelenburg position has a significant effect on the ZFP, the ZFP–CVP gradient should increase over time. Our observations show (Fig. 3A) that this gradient does not increase significantly ($P > 0.05$), even after 3 h of head-down positioning. This suggests that any cerebral perivascular oedema that may develop does not significantly hamper the cerebral perfusion.

The evolution of changes in cerebral vascular resistance can also be assessed by estimating the eCPP (Fig. 2).¹⁵ This eCPP should be slightly lower than the calculated CPP ($CPP = MAP - CVP$). As shown in Figure 3c, the eCPP is indeed slightly lower than the CPP, but the gradient between the CPP and the eCPP does not change significantly and neither the PI nor the RI increase significantly over the course of the operation (Fig. 3b). Moreover, the negative relationship between the ZFP and the $P_{E'CO_2}$ suggests that the CO_2 reactivity of the cerebral system is also preserved (Fig. 4). Although these variables of cerebral perfusion are influenced by multiple interdependent factors such as $P_{E'CO_2}$, positioning, PEEP, and muscle tone, these observations suggest that the cerebral microcirculation and cerebral autoregulation are preserved during the prolonged steep Trendelenburg positioning. This confirms the observations that the CBF– CO_2 reactivity is preserved in the modest Trendelenburg position with pneumoperitoneum during sevoflurane anaesthesia,¹⁸ and during

laparoscopic surgery in children.¹⁹ Moreover, it confirms that also in this more extreme clinical situation, CBF increases with a higher $P_{E'CO_2}$. Muscle tone and PEEP are thought to affect cerebral haemodynamics indirectly, by influencing the CVP and AP, and CPP and ZFP can be analysed directly as a function of CVP and AP. Inversely, the observation that the CPP, calculated as $CPP = MAP - CVP$, gives a very similar result to the eCPP¹⁵ (Fig. 2) suggests that even after prolonged steep Trendelenburg positioning, this time-honoured method of determining the CPP, based on the values of the MAP and CVP, remains valid.

This algorithm-based methodology to determine these ZFP, using a high-resolution regression analysis of synchronized pressure and flow waveforms, is the most mathematically and physiologically accurate. However, since this method is too elaborate to be clinically useful in routine practice, formula-based methods have been proposed and validated in several clinical conditions.⁵ These formula-based methods have not been validated in this particular clinical setting of combined extreme Trendelenburg position and CO_2 peritoneum. Therefore, together with a descriptive analysis of the evolution of the different brain flow variables over the course of the procedure, we also evaluated the validity of different formula-based methods in this clinical situation.

Throughout the whole procedure, $ZFP_{Czosnyka}$ was similar to ZFP_{reg} . In contrast, although $ZFP_{Schmidt}$ was similar to ZFP_{reg} during the pre-Trendelenburg period, it did not change significantly during Trendelenburg positioning, and remained at about one-third of the ZFP_{reg} (Fig. 3A). These results suggest that when patients are in this position, the method of Czosnyka provides a reliable estimate of ZFP whereas that of Schmidt does not. This allows more practical real-time monitoring of brain perfusion in this patient positioning. It also supports the thesis that the theoretical basis for this formula is a reliable reflection of the physiology.

As usual in clinical practice, the $P_{E'CO_2}$ varied between 4.0 and 7.0 kPa. The reliability of the derived ZFP-calculations can therefore only be confirmed within this range of $P_{E'CO_2}$. However, within this range, there is a tendency to increased ZFP at lower $P_{E'CO_2}$ (Fig. 4). This confirms that also in this patient positioning, it is commendable to avoid hyperventilation in order to optimize the lower limit of cerebral blood flow autoregulation.

In conclusion, even after prolonged combined steep Trendelenburg positioning and pneumoperitoneum, we found no evidence of increased resistance to cerebral blood flow other than that caused by the hydrostatic pressure due to the head-down position. The clinically convenient method to determine the ZFP described by Czosnyka remains valid, as does the conventional method for calculating CPP.

Declaration of interest

M.M.R.F.S. is a member of the editorial team of the *British Journal of Anaesthesia*. A.A. is a member of the Editorial Board of the *British Journal of Anaesthesia*.

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