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# Effect of lying position on cerebral hemodynamic and cerebral oxygenation in severe brain trauma patients

Geoffrey Dagod

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UNIVERSITE DE MONTPELLIER  
FACULTE DE MEDECINE MONTPELLIER-NIMES

**THESE**

Pour obtenir le titre de  
**DOCTEUR EN MEDECINE**

Présentée et soutenue publiquement  
Par

**Geoffrey DAGOD**

Le **9 octobre 2018**

**Effect of lying position on cerebral hemodynamic and cerebral oxygenation in severe brain trauma patients**

Directeur de thèse : Dr ROUSTAN Jean-Paul

**JURY**

Président : Pr CAPDEVILA Xavier

Assesseurs : Pr JABER Samir

Pr PERRIGAULT Pierre-François

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## **BACKGROUND**

Traumatic brain injury (TBI) remains a major public health and socio-economic problem throughout the world. The imputable mortality of severe TBI is indeed estimated between 7 to 39% depending on series (1,2). Moreover, TBI is known to be responsible for a substantial rate of lifelong disability in survivors. A French study has for example showed that only 7% of patients affected by a severe TBI experienced a return to quasi-normal life (3). A better knowledge of initial physio-pathological mechanisms and many advances would be thus necessary to hope improving the global outcome of severe TBI (TBIs).

Among the main recommendations during initial management of TBI (4), most experts agree on the maintaining of 30 degrees' head-up position, also called half-seated position, in order to optimize cerebral venous drainage and reduce intracranial pressure (ICP). This strategy is however supported by low number of studies, which were performed in the 1990s (5-10). These-ones were mostly focused on the analysis of ICP level, without consideration of all the perfusion parameters and cerebral oxygenation criteria (global and regional). Variations of cerebral physiological parameters between half-seated to lying positions were not considered in these previous studies, either. Moreover, many evolutions in management and therapeutic strategy of severe TBI have occurred these 20 last year's (11).

In clinical practice, the temporary transitions from the half-seated position to the lying position are frequently necessary during initial management of patients with TBIs; transfers, CT-scan performing, venous access placement, surgical intervention or some nursing cares for example. Thus, supine positioning is traditionally known to be associated in TBIs with an ICP increasing (5,8-10,12-14). No study has however described negative impact on cerebral perfusion or oxygenation during these transitory position changes. Besides, in a physiological point of view, the ICP increasing in lying position could not mean an alteration of cerebral haemodynamic conditions. ICP value is indeed not a good reflect of cerebral perfusion quality. We know that what matters is rather the cerebral blood flow (CBF) and his adequacy with cerebral metabolism to optimize cerebral oxygenation. It has been reported that the lying position may improve CBF and cerebral perfusion pressure (CPP) (15-17). In addition, cerebral autoregulation frequently altered during the initial phase of TBI (18-22) is probably an important determinant of cerebral perfusion variations between half-seated and lying position. No data is unfortunately available on this specific concern in literature. It seemed therefore relevant to observe cerebral physio-pathological



phenomena upon lying position during initial management of TBIs in order to better understand ICP increasing and its potential adverse consequences.

The aim of present study was to assess in patients with a severe TBI the impact of the temporary changeover from the half-seated position to the lying position on cerebral perfusion and oxygenation parameters during the first week of management. This analysis was especially performed according to the cerebral autoregulation status or neurologic outcome.

## **METHODS**

### *Study design and setting*

Between September 2014 and October 2016, we conducted a prospective, observational, monocentric study in the trauma intensive and critical care unit of Lapeyronie University Hospital (Montpellier, France), Regional Level 1 Trauma Centre.

### *Studied population*

Patients admitted in our unit with a severe TBI (Glasgow Coma Scale  $\leq 8$  associated with significant injuries of CT-scan) managed with an ICP monitoring were included in present study. Exclusion criteria were as follows: (1) penetrating mechanism; (2) age  $< 18$  years; (3) admission from another institution; (4) early death within 24 hours; (5) early decompression craniotomy; (6) pre-existing neurological or psychologic disease.

### *Ethical considerations*

Present study was carried out after approval by the Institutional Ethical Committee (ID RCB 2014-A00708-39) as well as the French data protection authority (CNIL) and is registered on ClinicalTrials.gov (NCT02832908). A written consent was obtained from all patients' family.

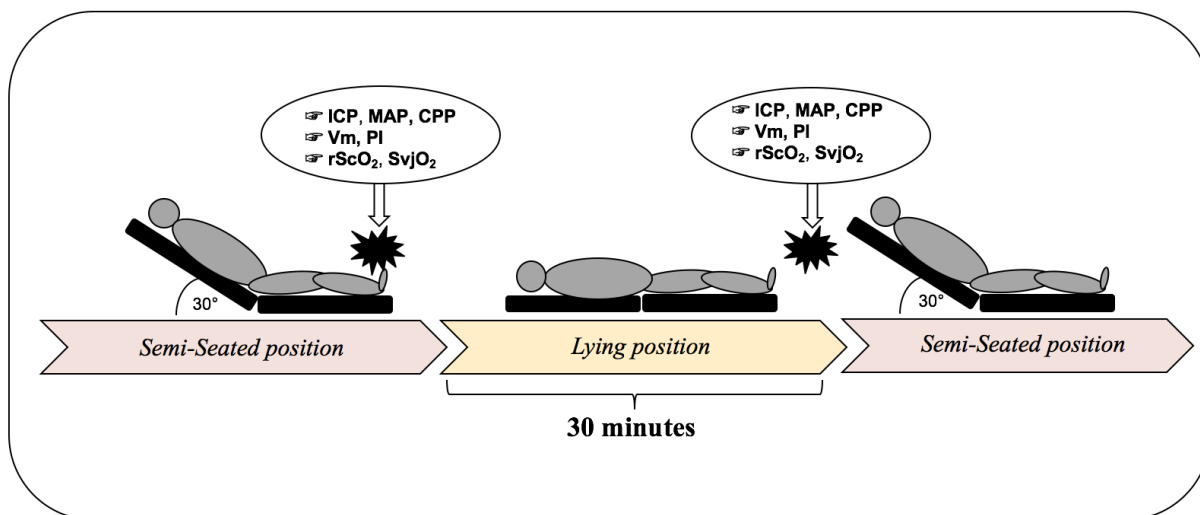
### *Management of patients*

During study period, severe trauma patients benefited in our unit of a standardized management according to the international guidelines (4). Patients affected by a severe TBI were thus sedated and mechanically ventilated in first days of management. The half-seated position with 30° elevations of trunk and head in the axis was applied from admission to the end of critical

phase. A multimodal monitoring was systematically used to guide management, including electrocardiogram, pulse oximetry, capnography, invasive arterial blood pressure (ABP) and ICP monitoring. A cerebral CT-scan assessment was carried out upon admission in all patients, with a systematic control within the 24 to 48 hours. The performing of other cerebral CT-scans could be proposed according to clinical evolution and acute worsening signs.

### *Study protocol and data collection*

For present study, a positioning manoeuvre was daily performed for each included patient during the 7 first days of hospitalization. This daily manoeuvre involved to a temporary changeover of patients in lying position with 0° of head elevation for a period of 30 minutes. Patients were then re-ascent in half-seated position (Figure 1). Measurements and data collection were achieved in stable hemodynamic conditions. No drug therapeutic or respiratory management likely to modify the hemodynamic brain conditions were undertaken during these manoeuvres, while remaining in the therapeutic objectives according to the guidelines. Realisation of positioning manoeuvres were interrupted in case of hemodynamic instability, material unavailability or good evolution with extubation.



**Figure 1.** Study protocol and timing of data collection (daily procedure)

The following data were collected each day, both before the positioning manoeuvre (half-seated position), and after 30 minutes of lying position (Fig. 1): pressure levels (ABP, ICP, Cerebral Perfusion Pressure [CPP], Central Venous Pressure [CVP]), cerebral oxygenation parameters (regional Saturation in Oxygen [rScO<sub>2</sub>] and venous jugular saturation in Oxygen [SvjO<sub>2</sub>]), transcranial Doppler (TCD) velocities on the middle cerebral artery (mean velocity [V<sub>m</sub>],

pulsatility index [PI]), under-aortic velocity-time integral (VTI) measured by transthoracic cardiac echography, arterial gazes and temperature.

To determine daily the cerebral autoregulation status, pressure reactivity index (PRx) was determined daily before positioning manoeuvres as follows (23): one-minute recording of ICP and ABP curves was collected every 3 minutes during a period of 2 hours before positioning maneuvers by a home-made signal analysis program (LabVIEW™ software, version 10.0, national instrument r, Austin, Texas), directly captured from monitor (Carescape™ Monitor B650, GE healthcare). After analogical antialiasing filtering, PRx was thus calculated as the moving Person correlation coefficient between consecutive values of couple ABP–ICP (23).

In addition, with previous data, the main demographic, admission clinical and biological data were recorded for each patient. Abbreviated Injury Scale (AIS) for each anatomic area (head, thorax, abdomen, pelvis and extremities) and the Injury Severity Score (ISS) were calculated (24,25). Finally, main outcomes of patients were determined: mortality at Day 30, Glasgow Outcome Scale at 6 months (GOS), duration in mechanical ventilation and length of stay (LOS) in Intensive Care Unit (ICU).

### *Study definitions*

ABP was measured in the radial or femoral artery and zeroed at the level of the right atrium (to obtain ABP) or at the level of the Monro foramen (to calculate CPP). ICP was measured by using a parenchymal probe inserted in the right frontal lobe and referenced at the level of the Monro foramen. CPP was defined as the difference of mean arterial pressure (MAP) and ICP.

Some cerebral variables (PI,  $V_m$  and  $rS_{cO_2}$ ) have been measured separately both right and left side. For these variables, the mainly-injured side was defined on the CT-scan, whereas the other side was qualified of less-injured side. In case of bilateral and symmetric injuries, the mainly-injured side was right side.

An impaired cerebral autoregulation was defined by a PRx >0.13 (26).

Finally, the clinical outcome was assessed using the GOS at 6 months (27). Unfavourable outcome was defined as dead, a persistent vegetative state and a severe disability (*i.e.*, GOS scores of 1, 2 and 3). Favourable outcome was in contrast defined as moderate disability or good recovery (*i.e.*, GOS 4 and 5).

## *Statistical analysis*

Continuous variables were expressed as median (interquartile range [IQR]) or mean  $\pm$  standard deviation (SD) according to their Gaussian distribution. The normality of the distribution of quantitative variables was determined using the Shapiro-Wilk test. Categorical were expressed as number (percentage). Comparison of variables between the lying position and the half-seated position at Day 1 was allowed using the paired *t*-test or a Wilcoxon tests according to their distribution. Thereafter, in order to highlight the influence of position over time, linear mixed models for repeated measures were performed. Each dependant variable (ICP, CPP, PI,  $V_m$ ,  $Sv_jO_2$  and  $rScO_2$ ) was analysed in a separate model. Position and day were considered as fixed effect and the patient as random. Explicative variables tested in multivariate mixed model were: CPP, ICP, mainly-injured side, temperature,  $PaCO_2$ , CVP, autoregulation status, osmolality and VTI. Intercept and slope were also tested. Effect estimates ( $\beta$ ) of significant variables are presented with corresponding 95% confidence interval (95% CI) and corresponding *P*-value. Models fit was assessed using the Bayesian Information Criterion (BIC). All reported p-values are two-sided, and a p-value of 0.05 was considered the threshold of statistical significance. Statistical analysis was performed using SAS software (SAS Enterprise Guide 7.1; SAS institute, Cary, NC).

## **RESULTS**

### *Patients characteristics and outcome*

During a 2-years period, 25 patients were enrolled in the first 24 hours after severe TBI. One patient was subsequently excluded because of a premature death within first 24 hours. The Baseline characteristics upon admission are presented in Table 1. The main mechanisms of trauma were motor-vehicle and motorcycles collisions (71%), falls (21%) and collided pedestrians (8%). The studied population was mostly males (92%), with a median age of  $39 \pm 16$  years, a median ISS score 32 (IQR, 25–48), a median SAPS II 50 (IQR, 40–59) and median Glasgow Coma Scale was 6 (IQR, 3–8).

The median ICU length of stay for the study population was 28 days (IQR, 21–45 days) and median mechanical ventilation duration was 20 days (IQR, 11-25 days). Three patients (16%) died (1 patient died of a multiple organ failure due to a mesenteric infarct, 1 died after the end of therapeutics because of a prolonged vegetative state and 1 patient died of a septic shock). Finally, 8 patients (33%) were defined as having an unfavourable outcome: 3 patients with a GOS 1 and 5 with a GOS 3.

### *Performing of study protocol*

A total number of 119 positioning manoeuvres were thus analysed in 24 patients; eight patients (33%) benefited from 6 or 7 consecutives daily positioning manoeuvres, and 7 (29%) others benefited from 5 manoeuvres. The 9 remaining patients experienced a lower number of manoeuvres. The main reasons of premature termination of the protocol were: premature death, unstable conditions before the manoeuvres, fast good evolution and technic difficulties. All positioning manoeuvres were performed as well. No one had to be prematurely interrupted for bad tolerance, intracranial hypertension or clinical signs of cerebral herniation. During the lying position, an ICP >22mmHg was observed in 16 tests (13%) in 9 patients without any clinical consequences. All SvjO<sub>2</sub> values were above the critical threshold for ischemia (50%) in both positions.

### *Impact of lying position at Day 1*

In half-seated position, the median ICP was 13 mmHg (IQR, 11–16 mmHg) and CPP was 61 mmHg (IQR, 53–67 mmHg). Following 30 minutes in lying position, ICP, CPP and MAP were significantly increased compared to half-seated position (Table 2), while under-aortic VTI did not change between 2 positions ( $P=0.21$ ). A significant raising of  $V_m$  was also observed in lying position, be it on mainly-injured side (+6 cm/s [IQR, +0–11 cm/s];  $P=0.01$ ) as on less-injured side (+4 cm/s [IQR, +1–8 cm/s];  $P<0.01$ ). Similarly, rScO<sub>2</sub> was significantly increased in lying position on both sides (+2 points [IQR, +2–4 points] and +3 points [IQR, +2–5 points], respectively;  $P<0.001$ ). Twenty patients (83%) thus experienced an increasing of rScO<sub>2</sub> in lying position. In parallel, a decrease of PI was observed in lying-position (-0.1 [IQR, -0.3–0];  $P=0.02$ ). SvjO<sub>2</sub> was slightly higher in lying position, but the difference was not significant ( $P=0.21$ ).

### *Impact of time course on cerebral variations*

In the seven days following the inclusion, the observed variation of ICP, CPP and ABP between two positions could be considered as clinically constant (Figure 2). As expected, multivariable analysis confirmed the significant relationship between the position and the value of ICP ( $\beta$ , 6.7 [95% CI 5.8 to 7.3];  $P<0.001$ ) with increased values in lying position. However, mixed models highlight the strong association between the position and the values of CPP ( $\beta$ , 6.6 [95% CI 4.7 to 8.8];  $P<0.001$ ),  $V_m$  ( $\beta$ , 5.0 [95% CI 2.0 to 7.8];  $P=0.001$ ), rScO<sub>2</sub> ( $\beta$ , 2.4 [95% CI 0.9 to 3.9];  $P=0.002$ ) and PI ( $\beta$ , -0.1 [95% CI -0.2 to -0.5];  $P<0.001$ ), with a more favourable conditions in the lying position. These findings were observed whatever the day in the first week after head

injury (Table 3). In addition, no significant difference of under-aortic VTI were found between the two positions over time (Figure 3).

### *Influence of cerebral autoregulation and outcome*

An impaired cerebral autoregulation was observed in 17 patients (71%) during first week, with a median PRx 0.45 (range 0.14-0.88). Seven (29%) as soon Day 1. Finally, 34 of 119 (29%) positioning manoeuvres were performed with an impaired cerebral autoregulation. The rate of favourable outcome did not differ between patients who experienced an impaired cerebral autoregulation and others (72% [13/18] versus 67% [4/6] respectively,  $P=1$ ). Variations of ICP, CPP,  $V_m$ , PI,  $rS_cO_2$  and  $SvjO_2$  according to the cerebral autoregulation status are presented in Figure 4.

The integration of cerebral autoregulation status as aleatory effect in the multivariable mixed model analysis did not reveal significant influence of this variable on cerebral hemodynamic and oxygenation variations induced by positioning manoeuvres ( $P=0.20-0.58$ ) (Table 3). Mixed models including neurological outcome as fixed effect did not found significant statistical relationship either ( $P=0.27$ ).

	Good outcome (GOS 4-5)	Unfavourable outcome (GOS 1-2-3)	Overall
n (%)	16(67)	8(33)	24
<i>Demographic characteristics</i>			
Male (%)	15(63)	7(29)	22(92)
Age (years)	39±15	39±20	39±16
<i>Admission severity criteria</i>			
Head AIS	4(4-4)	4(4-4)	4(4-4)
SAPS II	48(39-55)	58(49-63)	50(40-59)
ISS	31(28-46)	34(24-48)	32(25-48)
Glasgow score	6(3-8)	6(2)	6(3-8)
Initial needs of osmotherapy	3(13)	2(8)	5(21)
<i>Mechanism of injury (n, %)</i>			
Bicycle/motorcycles	6(25)	1(17)	7(29)
Fall	4(17)	1(4)	5(21)
Motor vehicles crash	6(25)	4(17)	10(42)
Pedestrian	1(4)	1(4)	2(8)
<i>Associated injury (n, %)</i>			
Thoracic traumatism	13(54)	6(25)	19(79)
Orthopaedic traumatism	6(25)	4(17)	10(42)
Abdominal traumatism	7(29)	3(13)	10(42)
Pelvic traumatism	4(17)	0(0)	4(17)
Spinal traumatism	5(21)	3(13)	8(33)
<i>Initial transfusion needs</i>			
Massive transfusion	2(8)	0(0)	2(8)
<i>Initial surgical interventions (n, %)</i>			
Haemostatics procedures	2(8)	0(0)	2(8)
Non-haemostatics procedures	3(13)	0(0)	3(13)
Neurosurgery	1(4)	0(0)	1(4)
<i>Outcome</i>			
ICU LOS (days)	25(20-44)	44(23-62)	28(21-45)
Mechanical Ventilation duration	17(10-21)	25(21-37)	20(11-25)
GOS at 6 months	4(4-5)	3(1-3)	4(3-5)
Death at 6 months	0(0)	3 (13)	3(13)

Data are expressed as means (standard deviation), medians (quartiles) or as the number of patients (percentage) as appropriate. AIS = Abbreviated Injury Scale; ISS = Injury Severity Score; SAPS = Simplified Acute Physiology Score; ICU = Intensive Care Unit; LOS = Length of stay; GOS = Glasgow Outcome Scale;

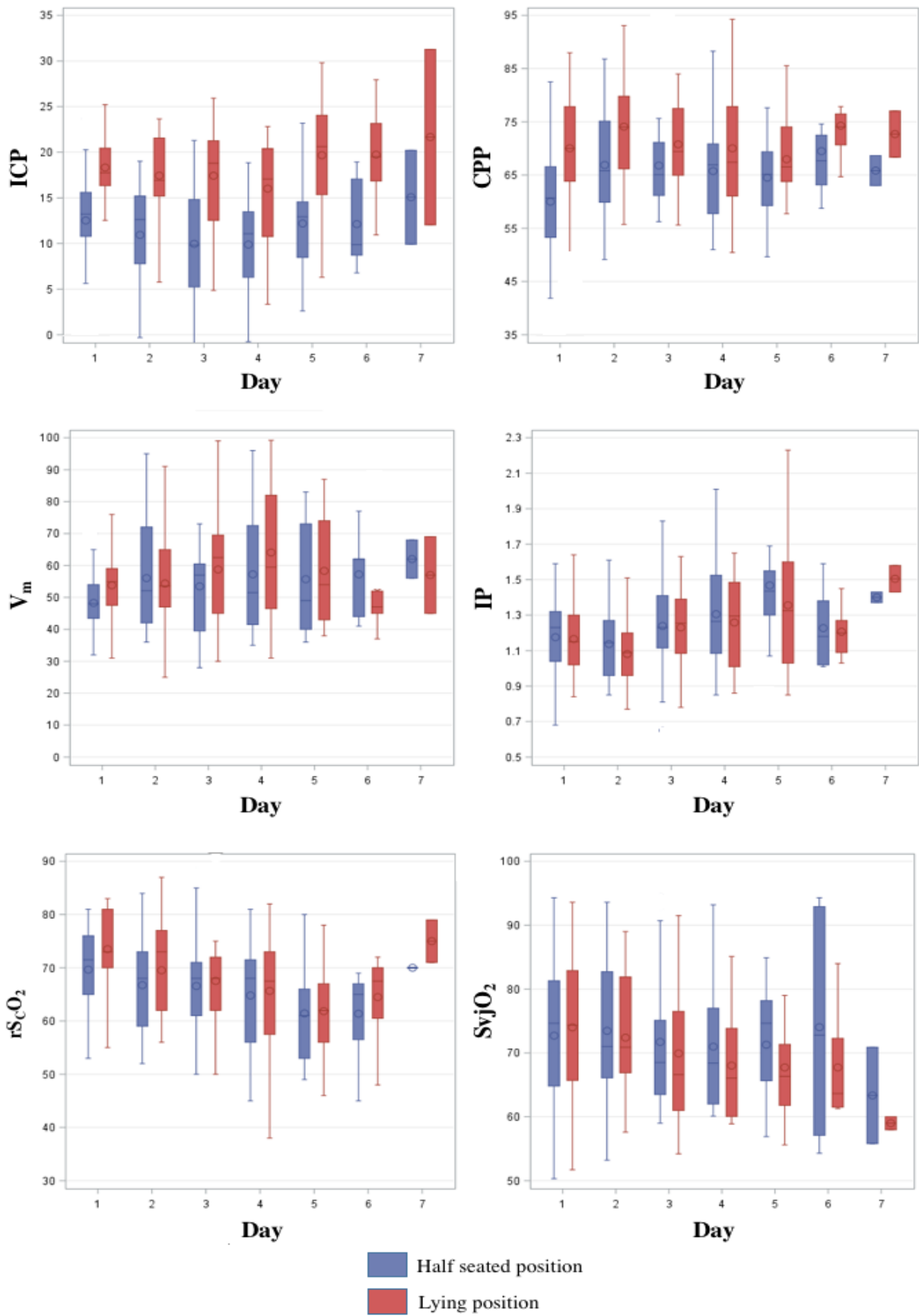
**Table 1.** Baseline characteristics at admission and outcome data

Parameters	Position		Variation in lying position	P
	Half-seated	Lying		
Intracranial pressure, mmHg	13 [11-16]	18 [16-20]	+6 [4-7]	<0.01
Cerebral perfusion pressure, mmHg	61 [53-67]	70 [64-78]	+10 [5-14]	<0.01
Mean arterial pressure, mmHg	80 [76-90]	90 [78-98]	+6 [1-10]	< 0.01
Mean velocity MIS, cm/s	48 [44-54]	55 [47-59]	+6 [0-11]	< 0.01
Mean velocity LIS, cm/s	49 [41-56]	55 [44-61]	+4 [1-8]	< 0.01
Pulsatility index MIS	1,2 [1-1,3]	1,2 [1-1,3]	0 [-0,1-0,1]	0.79
Pulsatility index LIS	1,2 [1-1,5]	1,1 [1-1,3]	-0,1 [-0,3-0]	0.02
Regional cerebral saturation in oxygen MIS, %	72 [65-76]	73 [70-81]	+2 [2-4]	< 0.01
Regional cerebral saturation in oxygen LIS, %	73 [63-75]	73 [70-81]	+3 [2-5]	< 0.01
Jugular venous saturation in oxygen, %	75 [65-81]	74 [68-78]	+1 [0-5]	0.21

Data are expressed as medians (Interquartile); IQR = Interquartile; MIS = Mainly Injured Side; LIS = Less Injured Side. Comparisons between the 2 positions was allowed using the paired *t*-test or a Wilcoxon tests according to their distribution

**Table 2.** Impact of lying position on intracranial pressure and mains cerebral perfusion and oxygenation parameters on Day 1





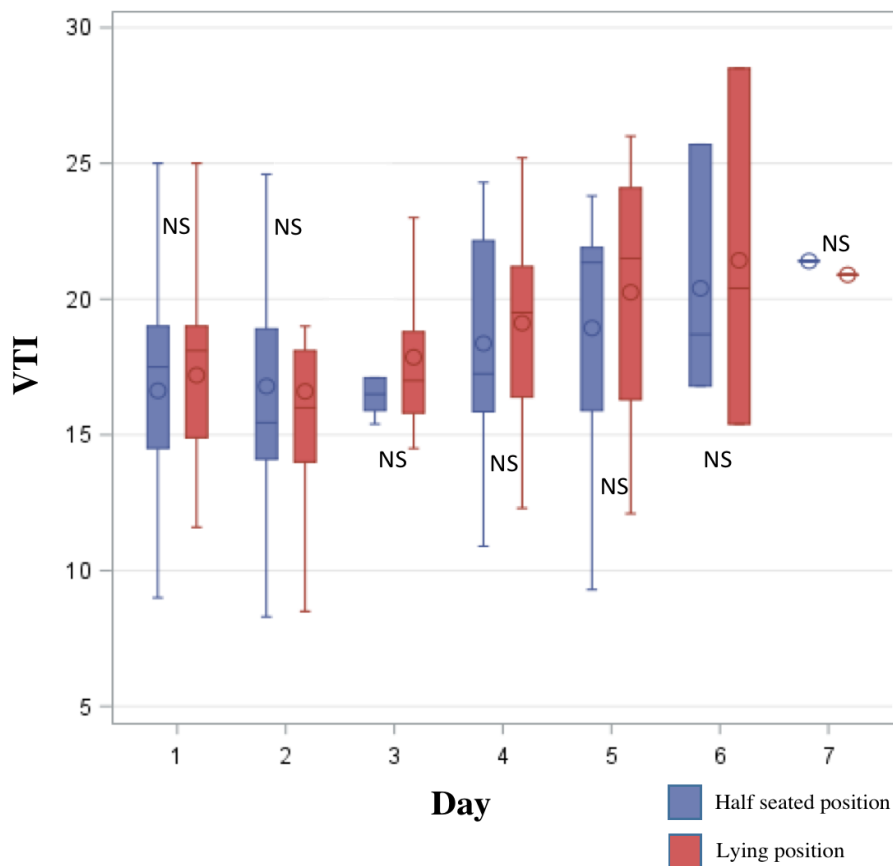
**Figure 2.** Cerebral effects of the changeover from half seated position to the lying position in the first week after severe TBI.

Dependant Variables	Lying position effect			Cerebral autoregulation effect		
	$\beta_{\text{lying}}$	95% CI	<i>P</i>	$\beta_{\text{AR}}$	95% CI	<i>P</i>
ICP	+ 6.7	5.8 to 7.3	<0.001	- 1.6	-0.9 to 4.1	<b>0.20</b>
CPP	+ 6.6	4.7 to 8.8	<0.001	+ 1.3	-4.8 to 2.2	<b>0.45</b>
$V_m$	+ 5.0	2.0 to 8.0	<b>0.001</b>	+ 3.2	-10.2 to 3.9	<b>0.37</b>
PI	- 0.1	-0.2 to -0,1	<0.001	0.0	-0.1 to 0.0	<b>0.24</b>
rScO <sub>2</sub>	+ 2.4	0.9 to 3.9	<b>0.002</b>	- 1.4	-1.8 to 4.6	<b>0.38</b>
SvjO <sub>2</sub>	+0.12	-1.2 to +1.5	<b>0.8</b>	+ 1.6	-7.4 to 4.2	<b>0.58</b>

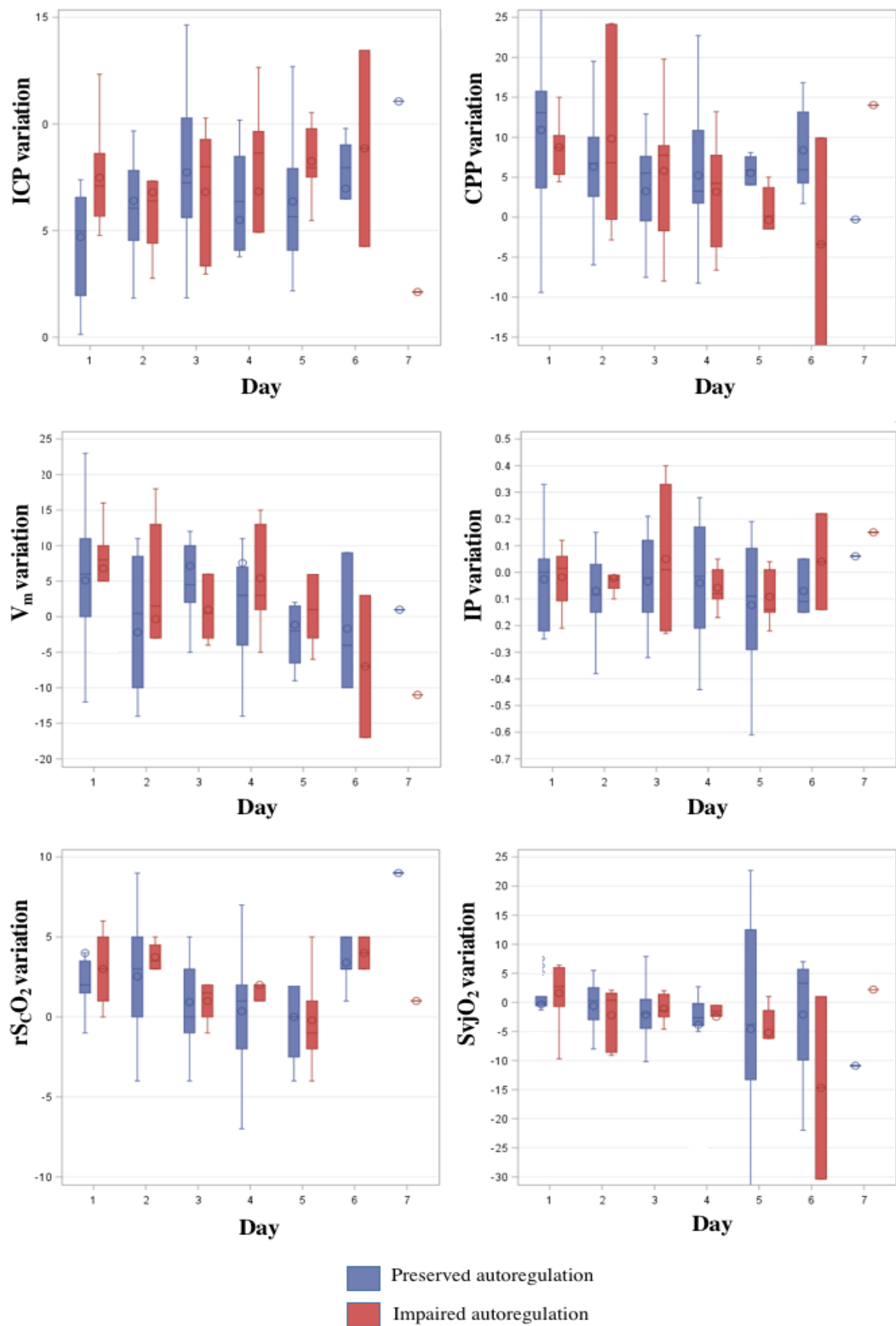
Explicative Variables tested in the multivariate analysis: day after trauma, CPP, VTI, osmolarity, ICP, Hb, pCO<sub>2</sub>, CVP, pH, natremia, autoregulation status, lesion side.

ICP = Intracranial pressure; CPP = Cerebral perfusion pressure;  $V_m$  = Mean velocity of middle cerebral artery; PI = Pulsatility index; rScO<sub>2</sub> = Regional saturation in Oxygen; SvjO<sub>2</sub> = Venous jugular saturation in Oxygen; CI = Confidence interval.

**Table 3.** Estimate effect of lying position ( $\beta_{\text{lying}}$ ) and cerebral autoregulation ( $\beta_{\text{AR}}$ ) of mains dependant cerebral variables (final mixed models).



**Figure 3.** Change in under-aortic VTI (velocity-time integral) over time between the half-seated position and after 30 minutes in lying position. A paired-t-test was used to compare VTI between the 2 position for each day.



**Figure 4.** Boxplots showing the variations in lying position of ICP, CPP, rScO<sub>2</sub>, V<sub>m</sub>, PI and SvjO<sub>2</sub> according to the autoregulation status (preserved or impaired)

## DISCUSSION

In this prospective cohort of 24 patients with severe TBI admitted to our trauma centre, the median duration of mechanical ventilation was 20 days and the rate of unfavourable outcome were 33%. Our work observed expected results on the behaviour of pressure levels upon lying positioning, with an ICP increasing, in association with a CPP and MAP rising. However, present study also highlighted a statistical increasing of  $V_m$  and  $rScO_2$  in lying position, in association with a decreasing of PI. No significant change of  $SvjO_2$  was in contrast observed between two positions. These findings were furthermore found regardless of the day in first week following trauma, cerebral autoregulation status or outcome.

Many studies in literature are focused on the consequences of head position during acute management of TBIs, which is well known to influence intracranial rheological conditions. The lying position may indeed induce many physio-pathological modifications (28): first, an increasing of venous and cerebrospinal fluid volumes leading to a drop of cerebral compliance. Second, a change on venous return ways, with a predominance of internal jugular veins more subject to variation of thoracic pressure rather than vertebral venous plexus. Third, a rising of arterial blood pressure at the brain level by simple hydrostatic effect, involving autoregulation phenomena; either a vasoconstriction or a vasodilatation may thus occur according to cerebral autoregulation status. All these mechanisms may therefore participate in a higher ICP in lying position and a drop of cerebral compliance.

The temporary transition from the half-seated position to the lying position is anyway frequently necessary during initial management of patients with severe TBI (*e.g.*, transfers, CT-scan performing, venous access placement, surgical intervention or nursing cares). Thus, the increasing of ICP observable in lying position could logically be thought as a sign of brain suffering. However, no study has clearly demonstrated worst impact of lying position on an injured brain. Innovatively, our work has revealed that the ICP increasing during a temporary lying position did not reflect an alteration of cerebral hemodynamic conditions or cerebral oxygenation in the first week after TBI. In multivariate analysis (Table 3), we indeed showed that the changeover in lying position was associated with a significant increasing of TCD velocity on the middle cerebral artery in favour of an improvement of CBF. Furthermore, regional cerebral oxygenation estimated by  $rScO_2$  seemed also improved. These findings are concordant with other series that found a better CBF in lying position in patients affected by acute ischemic stroke (15). In parallel, no significant change in global cerebral oxygenation assessed by  $SvjO_2$  was found.

Three main hypotheses might thus be advanced at first glance to explain this increasing cerebral blood flow induced by the transitory lying position: An increasing of cardiac output induced by an optimized preload, an arterial pressure rising at the brain level caused by a simple hydrostatic phenomenon, and/or the consequences of impaired cerebral autoregulation. The mobilization in lying position induces automatically a blood volume transfer into venous compartment, which may lead to an optimization of cardiac preload. The cardiac preload change could thus have induced in our series a systematic increasing of cardiac output generating the increasing of cerebral blood flow, particularly in patients who lost cerebral autoregulation (29). Our data do however not support this mechanism: under-aortic VTI were indeed found comparable before and after the manoeuvres. It is probable that studied patients had an optimal blood volume status before the positioning manoeuvres.

Otherwise, an important point must also be considered when position changing of TBIs, the determination of zero level for invasive arterial pressure. Reference pressure level is obviously determinant since it will induce a systematic calculation mistake for CPP when cerebral and cardiac level are distinct. A simple trigonometric calculation reveals indeed a value difference of almost 10–15 mmHg between heart and head in a standard person with 30 degrees' elevation head and 30 cm distance (30). Thus, upon the changing toward the lying position, the CPP value will be artificially increased of this systematic bias with a stable arterial pressure if the reference pressure level to calculate CPP is established at the right atrium level. To avoid this systematic instrumental bias induced by the head position, many experts recommend therefore to consider the reference pressure level for CPP calculation at Monro foramen, using the tragus of the ear as external landmark (31). Nevertheless, it exists a lack of homogenization in literature on this specific point (30, 32). In our study, we chose to systematically determine the zero level for CPP calculation at the level of ear tragus to not be exposed to this instrumental bias.

Impaired autoregulation could be likewise involved in this positional change of cerebral blood flow. This would be indeed the consequence of a simple hydrostatic increasing of CPP caused by lying position associated with an incapacity of reflex arterial vasoconstriction. One supplementary strength of our work is therefore to have assessed the influence of cerebral autoregulation status before each positioning manoeuvres using the PRx (23). Surprisingly, our findings reveal that cerebral autoregulation status did not significantly influence changes of cerebral physiological conditions induced by the positioning. But observed variations of PRx over time show aleatory variations in time without any underlying physio-pathological phenomenon.

Thus, several reasons let us think that PRx calculation is questionable. First, there is mostly no direct causality between spontaneous variations of ABP and ICP because they are below the threshold of autoregulation involvement. Second, the triggering of cerebral autoregulation occurs within a period of 4 to 6 seconds. Thus, any quick variation of ABP (cough) will lead in a similar variation in ICP with an artificial increase in PRx value, regardless of the autoregulation status. Third, autoregulation applies only in a plateau (Lassen's curve) and then, any variations outside this plateau will lead to an increase in PRx value.

Based on our results, we suppose that the modest increasing of arterial blood pressure at the brain level by the hydrostatic effect lead to an increasing of CPP. It is also possible that the lying position could produce an improved use of collateral circulation in damaged areas. We however didn't show any differences according to the mainly injured side, but most of patients had bilateral lesions. Considering this slight increasing of CBF, it could seem surprising to not observe a concomitant increasing of SvjO<sub>2</sub> during our positioning manoeuvres. As the cerebral metabolic rate of oxygen remains stable between the 2 positions, the increase in CBF must result in an increase of SvjO<sub>2</sub>. We suppose that the important modifications of cerebral venous drainage pathways between two positions could explain our results and make the variations of SvjO<sub>2</sub> questionable during the manoeuvres. Indeed, SvjO<sub>2</sub> in lying position is more the reflection of the venous saturation in oxygen of facials veins than cerebral veins (28). SvjO<sub>2</sub> might thus be inaccurate in half-seated position, not reflecting cerebral extraction.

Present study has several potential limitations. First, the studied sample size is small that might induce an insufficient statistical power. The findings should therefore be as considered preliminary results. Second, most of brain trauma patients included in present study had other severe lesions with different lesioned mechanisms. This may introduce a selection bias. Third, patients were studied in stable conditions and early deaths were also excluded. Our findings cannot be consequently extrapolated to unstable or critical patients. Similarly, opening head trauma were excluded of our work because of a different physio-pathological behaviour. Fourth, our work assessed early consequences of the lying position in severe TBI (30 minutes). No conclusion should be therefore drawn for prolonged consequences of lying position. Fifth, TCD ultrasound may introduce some error because the measurements are operator dependent but it's widely accepted as a safe and reliable non-invasive technique for measuring CBF velocity. Consistency and accuracy in the present study were ensured by the use of two experienced operators. Although mean flow velocities do not equate CBF, it reflects it well, especially since diameter of ACM is

constant which is the case in our study, knowing that cerebral vasoreactivity occurs on vessels with a diameter of less than 200  $\mu\text{m}$ .

To conclude, present study showed that a moderate increasing of ICP upon a transitory lying positioning did not reflect an impairment of cerebral hemodynamic and cerebral oxygenation conditions in the first week after TBI. Transitory lying position was conversely accompanied by an increasing of CPP, blood flow velocities and  $r\text{ScO}_2$ . Our work did however not assess prolonged consequences of the lying position in these critically-ill patients.

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## SERMENT

- *En présence des Maîtres de cette école, de mes chers condisciples et devant l'effigie d'Hippocrate, je promets et je jure, au nom de l'Être suprême, d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la médecine.*
  
- *Je donnerai mes soins gratuits à l'indigent et n'exigerai jamais un salaire au-dessus de mon travail.*
  
- *Admis (e) dans l'intérieur des maisons, mes yeux ne verront pas ce qui s'y passe, ma langue taira les secrets qui me seront confiés, et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.*
  
- *Respectueux (se) et reconnaissant (e) envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.*
  
- *Que les hommes m'accordent leur estime si je suis fidèle à mes promesses. Que je sois couvert (e) d'opprobre et méprisé (e) de mes confrères si j'y manque.*

## ABSTRACT

**BACKGROUND:** Severe brain-injured patients are traditionally maintained in half-seated position (HSP). However, the temporary transitions from the HSP to the lying position (LP) are necessary during management of these patients. We sought to assess in patients with a severe TBI, the impact of the LP on cerebrovascular dynamics and global as well as regional cerebral oxygenation within first week.

**METHODS:** 24 patients with a severe closed TBI and managed with an ICP monitoring were included in our study. For each patient, a positioning manoeuvre of 30 minutes in LP was daily performed during the first week. Cerebral perfusion parameters (ICP, CPP, Vm, PI) and cerebral oxygenation parameters (rScO<sub>2</sub>, SvjO<sub>2</sub>) were compared in HSP (30°) and LP (0°). Mixed models were performed to highlight the effect of position on these variables.

**RESULTS:** On day 1 after the trauma, following 30 minutes in LP, ICP and CPP were increased compared to HSP (respectively +6 mmHg [4-7] and +10mmHg [5-14]). A raising of Vm was also observed in LP (+6 cm/s [0–11]; *P*=0.01) in association with a decrease of PI in LP (-0.1 point [-0.3-0]; *P*=0.02). Similarly, rScO<sub>2</sub> was increased in LP (+3 points [2-5 points]; *p*<0,001). Mixed models analysis confirms the association between the position and the value of CPP, Vm, rScO<sub>2</sub>, PI, with more favourable conditions in the LP. There was no influence of cerebral autoregulation status or neurologic outcome.

**CONCLUSION:** Moderate increasing of ICP during routine nursing care in LP did not reflect an impairment of cerebral hemodynamic and cerebral oxygenation conditions in the first week after TBI.

**KEYWORDS:** Brain trauma injury, Lying position, Cerebral hemodynamic, Cerebral oxygenation, Cerebral Autoregulation