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Relation entre pression de perfusion cérébrale et oxygénation cérébrale chez le patient traumatisé crânien grave et impact sur le devenir

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Sigles

ACSOS	Agressions cérébrales secondaires d'origine systémique
CaO_2	Contenu en oxygène du sang artériel afférent
CCI	*Charlson Comorbidity Index*
$CMRO_2$	Consommation cérébrale en oxygène
CPP	*Cerebral perfusion pressure*
CvO_2	Contenu en oxygène du sang artériel efférent
DAI	*Diffuse axonal injury*
DSC	Débit sanguin cérébral
EDH	*Extradural hematomas*
EVD	*External ventricular drainage*
FiO_2	Fraction inspire en oxygène
GCS	*Glasgow Coma Scale*
GOS	*Glasgow Outcome Scale*
HTIC	Hypertension intracrânienne
ICP	*Intracranial pressure*
IGSII	Index de Gravité Simplifié II
IVH	*Intraventricular hemorrhage*
MAP	Mean arterial pressure
NIRS	*Near infraRed spectroscopy*
ORx	*Oxygen reactivity index*
$PaCO_2$	Pression partielle en dioxyde de carbone dans le sang
PAM	Pression artérielle moyenne
PaO_2	Pression partielle en oxygène dans le sang
PIC	Pression intracrânienne

PPC Pression de perfusion cérébrale

PRx *Pression reactivity index*

$PtiO_2$ Pression tissulaire en oxygène

RVC Résistances vasculaires cérébrales

RVS Résistances vasculaires systémiques

SAH *Subarachnoid hemorrhage*

SAMU Service d'aide médicale urgente

SaO_2 Saturation de l'hémoglobine en oxygène

SDH *Subdural hematomas*

SIBICC Seattle International Severe Traumatic Brain Injury Consensus Conference

TBI *Trauma brain injury*

VO_2 Consommation en oxygène du tissu cérébral

Sommaire

Introduction

1 Introduction générale

Le traumatisme crânien grave est défini par un score de Glasgow inférieur ou égal à 8. [1]

Cette pathologie possède, toute gravité confondue une incidence estimée de 47 à 694 pour 100000 habitants par an, avec un taux de mortalité de 9 à 28 pour 100000 habitants par an en Europe. Cette affection touche majoritairement des sujets jeunes et masculins. [2]

Elle a pour conséquence des manifestations diverses tout au long de la vie, physiques, neuropsychologiques et sociales touchant jusqu'à 80% des patients. [3,4]

Les causes prépondérantes sont les chutes et les accidents de circulation. [2,5]

Le traumatisme crânien grave comporte un coût global important, estimé à plus de 22 milliards d'euros en Europe en 2012, pour les traumatismes crâniens modérés et graves. [8]

2 Mécanisme lésionnel

Indépendamment de la cause du traumatisme crânien, les lésions cérébrales provoquées par le choc entrainent des modifications cellulaires, moléculaires ainsi que du métabolisme cérébral provoquant une diminution de la délivrance et une augmentation de la consommation en oxygène, pouvant aboutir à la mort neuronale par ischémie. [6]

Les lésions cérébrales provoquées sont de deux natures différentes :

- Les lésions dites primaires, conséquences de l'atteinte neuronale initiale, de mécanismes multiples et hétérogènes. Il s'agit de contusions, de lésions axonales diffuses, d'hématomes extra et sous duraux, d'hémorragies sous arachnoïdiennes et intra-ventriculaires. Celles-ci nécessitent parfois une prise en charge neurochirurgicale à la phase initiale.
- Les lésions dites secondaires, issues d'une cascade de remaniements cellulaires et métaboliques, affectant des zones dites de « pénombre ». Ces lésions justifient de mettre en place immédiatement une oxygénation optimale et de lutte contre l'œdème cérébral via la gestion des agressions cérébrales secondaires d'origine systémique (ACSOS).

Les ACSOS se composent de :

- la capnie,
- l'oxygénation,
- la pression artérielle,
- les dysnatrémies,
- la glycémie,
- la température,
- l'hémoglobine,
- la volémie.

Anatomiquement, la boîte crânienne se compose de trois éléments : l'encéphale, le sang et le liquide céphalo-rachidien. Ces composants se situent dans un espace clos dont les parois osseuses sont peu élastiques.

Selon l'hypothèse de Monro-Kellie, le volume intracrânien est sensiblement constant, ainsi toute variation de volume de l'un ou de l'autre de ces secteurs doit s'accompagner d'une diminution de volume des autres. [7]

Ainsi, lors d'une augmentation de volume de l'encéphale causée par les lésions primaires ou secondaires, la perte d'élastance provoque une hypertension intracrânienne (HTIC).

L'HTIC possède une incidence élevée mais inégale, de l'ordre de 17 à 88%, avec des conséquences néfastes sur le pronostic vital et fonctionnel des patients, allant jusqu'à la mort encéphalique. [1,8]

Ce sont les lésions dites secondaires, potentiellement contrôlables au décours de la phase initiale qui influencent de manière importante le pronostic des patients. [9]

3 Autorégulation cérébrale

L'autorégulation cérébrale est la capacité intrinsèque du cerveau permettant de maintenir un environnement stable, avec des apports en oxygène et en nutriments constants par le biais d'un débit sanguin cérébral égal. Cela, malgré les modifications hémodynamiques de pression de perfusion cérébrale ou de pression artérielle. [10]

Le métabolisme cérébral étant aérobie avec des capacités de stockage faibles, l'oxygénation cérébrale dépend de ses apports et de sa consommation en oxygène, selon la relation :

$$DSC = VO_2 \times (CaO_2 - CvO_2)$$

- La VO_2 étant la consommation d'oxygène du tissu cérébral.
- La CaO_2 étant le contenu en oxygène du sang artériel afférent.
- La CvO_2 étant le contenu en oxygène du sang veineux efférent.
- La CaO_2 - CvO_2 étant la différence artério-veineuse en oxygène.

La CaO_2 est un paramètre régulé par le taux d'hémoglobine, la SaO_2 et la PaO_2.

Le débit sanguin cérébral (DSC) est déterminé par la pression de perfusion cérébrale (PPC), l'autorégulation cérébrale et les résistances vasculaires cérébrales (RVC), par la relation :

$$DSC = PPC / RVC$$

Lorsque le plateau d'autorégulation est préservé, une augmentation de la PPC entraîne une augmentation des RVC et inversement afin de préserver un DSC constant.

Les résistances vasculaires cérébrales dépendent des facteurs qui s'opposent à l'écoulement du sang dans les vaisseaux cérébraux, c'est à dire de la viscosité du sang, de l'état anatomique et fonctionnel du lit vasculaire, du tonus vasculaire des muscles lisses composant les résistances vasculaires systémiques ainsi que de la pression du liquide céphalo-rachidien.

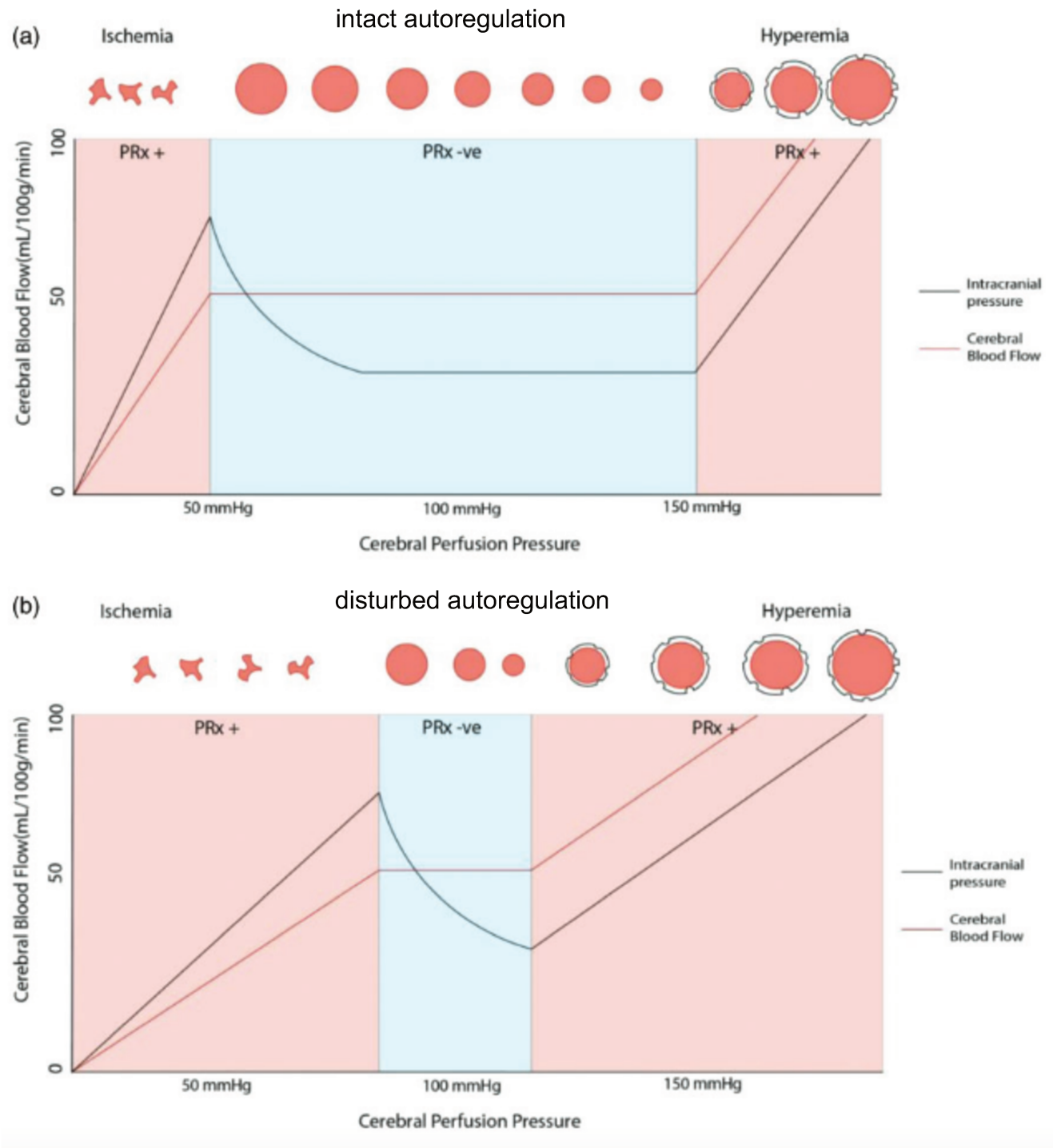

Figure 1 : Relation entre perfusion cérébrale et PPC en lien avec l'autorégulation cérébrale, d'après [11].

L'autorégulation cérébrale peut être altérée chez les patients traumatisés crâniens graves, ne leur permettant pas de répondre aux variations des conditions hémodynamiques.

La recherche du plateau d'autorégulation, donc d'une pression de perfusion cérébrale optimale est l'un des objectifs de la prise en charge. [12]

La perte de cette autorégulation cérébrale étant un facteur démontré d'ischémie cérébrale secondaire et de mauvais devenir neurologique. [13,14]

4 Principes du monitorage de l'hémodynamique cérébrale

L'évaluation clinique neurologique des patients dans le coma est complexe et d'interprétation délicate. La variation pupillaire étant un signe clinique tardif évocateur de lésions ischémiques probablement déjà constituées, imposant une surveillance continue.

La prise en charge du traumatisme crânien grave se fait via des paramètres indirects que le clinicien se doit d'analyser et d'intégrer à ses décisions thérapeutiques, basés sur le maintien de l'homéostasie cérébrale.

Les soins actuels de ces patients reposent sur une prise en charge multidisciplinaire et spécialisée en centres experts en neuro-réanimation avec un plateau technique adéquat.

Par ailleurs, il n'existe pas de thérapeutique médicamenteuse spécifique au traitement des lésions causées par le traumatisme crânien. [15,16]

Les sociétés savantes françaises et internationales recommandent d'utiliser, en plus du monitorage de la pression artérielle invasive et du taux sanguin en oxygène [17], un monitorage multimodal de l'hémodynamique cérébrale invasif et non invasif comme l'imagerie cérébrale, le doppler transcrânien, le NIRS. [1,9]

Afin d'optimiser l'oxygénation et le débit sanguin cérébral des zones de pénombre, deux types de monitorage invasif et continu sont utilisés et recommandés par les sociétés savantes, sans essai randomisé démontrant leur impact sur le devenir des patients traumatisés crâniens graves : la pression intracrânienne et la pression tissulaire en oxygène. [1,18]

5 La pression intracrânienne (PIC)

Historiquement, le monitorage des patients traumatisés crâniens reposait sur la mesure de la PIC et la surveillance de la PPC afin de prévenir les agressions cérébrales secondaires. [15]

Le monitorage de la PIC s'effectue via un capteur intra-parenchymateux ou intra-ventriculaire, permettant le dépistage de l'HTIC et le monitorage de la PPC, selon l'équation suivante :

$$PPC = PAM - PIC.$$

La PAM étant la pression artérielle moyenne.

La valeur physiologique de la PIC est aux alentours de 15 mmHg, avec des variations lors des efforts de toux par exemple. [19]

Cette pression est un déterminant majeur du débit sanguin cérébral et est considéré comme l'un des gold standard de son estimation. Elle est donc recommandée dans le monitorage du traumatisme crânien grave, avec un objectif de PIC devant être inférieur à 22 mmHg. [1,20]

Ce monitorage est relativement peu pourvoyeur de complications pour les capteurs intra parenchymateux avec environ 1% d'infections et d'hémorragies, contrairement

aux capteurs sur dérivations ventriculaires externes, qui peuvent être plus comorbides avec 10% et 30% respectivement. [21]

L'élévation de la pression intracrânienne est corrélée à un risque majoré de séquelles neurologiques et de mortalité. Une revue systématique de la littérature rapporte un surrisque de mortalité par 3 lorsque la PIC se situe entre 20 et 40 mmHg et par 7 lorsqu'elle est au-dessus de 40 mmHg. [8]

Néanmoins, des épisodes d'ischémies et d'hypoxies cérébrales sont fréquents après un traumatisme crânien, indépendamment d'une PIC normale. [22]

6 La pression tissulaire en oxygène ($PtiO_2$)

La $PtiO_2$ correspond à la pression en oxygène du parenchyme cérébral mesurée sur un volume donné.

La sonde est le plus souvent introduite dans la substance blanche du lobe frontal droit chez les droitiers, associée à une sonde de PIC.

Cette mesure s'effectue via une électrode de Clark intra parenchymateuse, contenant une anode et une cathode recouverte d'une membrane perméable aux gazes, dans une solution aqueuse d'électrolytes. Un courant continu est produit via la réduction par la cathode d'une molécule d'oxygène dissous, produisant un électron selon cette relation d'oxydo-réduction. Ce courant électrique est proportionnel à la concentration en oxygène, exprimé en pression par le moniteur. Elle associe une mesure de la température. [23]

Cette mesure relativement simple à mettre en place au lit du patient, complémentaire à la mesure de la PPC, permet d'améliorer la compréhension des dysfonctions

cérébrales après un traumatisme crânien, mais également de détecter de manière précoce une ischémie et une hypoxie cérébrale. [23]

Elle reflète l'apport et la diffusion de l'oxygène dans le milieu interstitiel cérébral, localisé dans une région de 7 à 15 mm3 aux pourtours de la sonde.

Bien qu'il s'agisse d'un monitorage invasif, c'est une technique relativement peu comorbide. Dans une cohorte de 123 patients, il est retrouvé 14 saignements intracrâniens (11%), dont 1 ayant nécessité une intervention de drainage. [24]

Sa valeur dépendrait du débit sanguin cérébral et du métabolisme cérébral [5]. Dans le cadre d'une agression cérébrale, l'œdème généré semble limiter la diffusion de l'oxygène vers les tissus et ainsi créer des régions ischémiques. [9]

Le traumatisme crânien augmente la consommation en oxygène cérébrale ($CMRO_2$) mais peut également altérer sa distribution, directement ou par effet d'hypo et d'hypertension artérielle, de bas débit cardiaque, d'hypocapnie, d'hypoxémie, d'anémie ou d'hyperthermie.

L'oxygénation cérébrale peut varier par des facteurs intrinsèques comme la pression de perfusion cérébrale, la $CMRO_2$ et par des facteurs extrinsèques comme la PaO_2 et l'hémoglobine.

Ainsi, la PaO_2, $PaCO_2$, le taux d'hémoglobine, la dose de noradrénaline modifiant les RVS et l'emplacement de la sonde de $PtiO_2$ (en zone saine ou péri contuse) doivent être connus pour son interprétation. [1,25]

Une $PtiO_2$ optimale, supérieure à 20 mmHg, serait responsable d'une diminution de la mortalité et d'un pronostic neurologique favorable, alors qu'une $PtiO_2$ basse, inférieure à 15 mmHg, et la durée de celle-ci, seraient un facteur pronostique neurologique défavorable, hors modifications de pression de perfusion cérébrale. [9,20,26]

La mesure de la $PtiO_2$ est un outil qui pourrait permettre de déterminer un objectif de pression de perfusion cérébrale optimale, en établissant une pression de perfusion cérébrale minimale avec une $PtiO_2$ au-dessus du seuil ischémique. [26,27]

Figure 2 : Déterminants de l'oxygénation cérébrale, d'après [11]

Dans la littérature, l'intérêt du monitorage de la $PtiO_2$ n'est pas parfaitement démontré. Son effet sur la mortalité et le devenir neurologique serait indépendamment associé au monitorage par PIC et doppler transcrânien dans des études rétrospectives. [28–32]

Une étude rétrospective américaine met en évidence une diminution de la mortalité des patients lorsque le monitorage associe la PIC à la $PtiO_2$ contrairement à la PIC seule, sans différence sur le devenir neurologique. [33]

Il est retrouvé dans une étude prospective une meilleure détection des épisodes d'ischémies par monitorage multimodal intracrânien (PIC, $PtiO_2$ et microdialyse cérébrale) comparé à la PIC seule. [34]

Dans les études randomisées multicentriques, son intérêt n'est pas encore parfaitement démontré, ainsi son utilisation repose sur des avis d'experts. [22,35–37]

Néanmoins ces éléments sont repris dans les dernières recommandations internationales. [18,20]

7 Implications pratiques

L'hypoxie cérébrale pouvant se produire même sans épisode d'HTIC, les stratégies de contrôle de PIC s'accompagnent d'un contrôle de la délivrance cérébrale en oxygène.

Les recommandations internationales de la Brain Trauma Fundation et du SIBICC s'accordent pour obtenir une pression de perfusion cérébrale entre 60 et 70 mmHg à la phase initiale et inférieure à 90 mmHg avec une PIC < 22 mmHg et une $PtiO_2$ > 20 mmHg. [18,20]

Un algorithme proposé par le SIBICC en 2020 évoque les actions possibles en fonction des quatre phénotypes possibles de PIC et de $PtiO_2$.

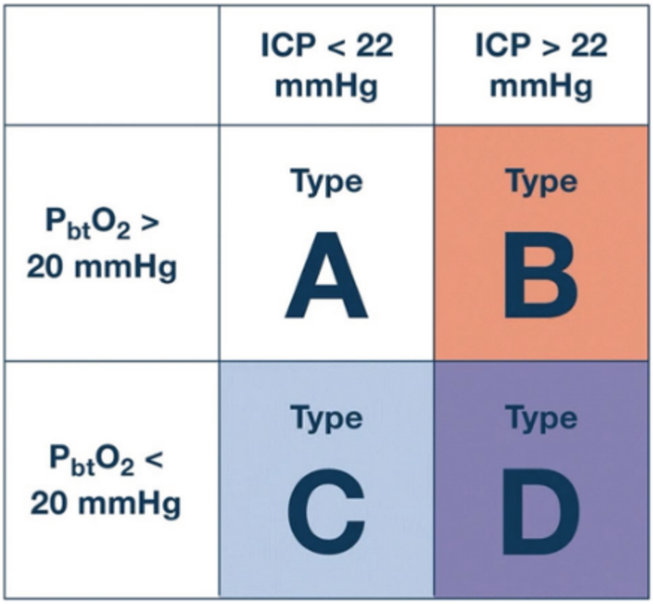

Figure 3 : Phénotypes de monitorage de traumatisme crânien en utilisant la PIC et la $PtiO_2$, selon le SIBICC [18]

En fonction de ces phénotypes, plusieurs thérapeutiques peuvent être mises en place (liste non exhaustive et non hiérarchique) :

- Augmentation de la PAM
- Augmentation de la PaO_2
- Hyperventilation alvéolaire et baisse de la capnie
- Augmentation de l'hémoglobine
- Osmothérapie
- Mise en place d'une dérivation ventriculaire externe
- Augmentation des sédations pouvant aller jusqu'au coma barbiturique
- Curarisation
- Hypothermie
- Craniectomie décompressive

La prise en charge du patient traumatisé crânien grave est complexe et hétérogène. Les données du monitorage multimodal permettraient d'adapter chaque patient en fonction des données de PIC, de PPC et d'autorégulation cérébrale. Ainsi, de guider la prise en charge thérapeutique.

8 Objectif

Les études évaluant la relation entre la $PtiO_2$ et la PPC ne concernent qu'un nombre restreint de patients. [10]

Nous faisons l'hypothèse qu'à $PaCO_2$, PaO_2 et hémoglobine égales il existe une relation linéaire entre la PPC et la $PtiO_2$ et donc que la $PtiO_2$ est un reflet direct du débit sanguin cérébral.

L'objectif principal de ce travail est d'analyser la relation entre la $PtiO_2$ et la PPC ainsi que l'impact de la $PtiO_2$ sur le devenir des patients traumatisés crâniens graves.

Article en Anglais

1 Introduction

Severe trauma brain injury (defined as a Glasgow Coma Scale (GCS) of less than or equal to 8 [1]) is frequent and mainly affects young male subjects [2]. With an incidence of 47 to 694 per 100.000 habitants per year and a mortality of 9 to 28 per 100.000 habitants per year in Europe, it is a disease with a high overall cost and a high impact on quality of life. [3,4]

Brain lesions caused by trauma, whether primary or secondary, lead to cellular, molecular and metabolic changes in the brain. These changes result in a reduction in oxygen delivery and an increase in oxygen consumption, which can lead to neuronal death due to ischemia. [6]

Primary lesions are targets for neurosurgical treatment, while secondary lesions can be prevented with appropriate management, including aggressive management of secondary systemic brain injury.

The Guidelines recommend the use of invasive and noninvasive multimodal monitoring [1,9] to optimize cerebral oxygenation and cerebral blood flow. Two types of invasive and continuous monitoring are used and recommended, but there are no clinical studies demonstrating their impact on patient outcome : intracranial pressure (ICP) and tissue oxygen pressure ($PtiO_2$). [1,18]

Episodes of cerebral ischemia and hypoxia are common after head injury, regardless of normal ICP [22] . Monitoring $PtiO_2$ would allow oxygen consumption to be adapted to demand.

Measuring $PtiO_2$ could help determine an optimal cerebral perfusion pressure target, establishing a minimum cerebral perfusion pressure with a $PtiO_2$ within the normal range described in the literature. [26,27]

The optimal value of $PtiO_2$ monitoring has not been fully demonstrated. Its effect on mortality and neurological outcome would be independently associated with ICP and transcranial Doppler monitoring in retrospective studies. [28–32]

A retrospective American study showed a reduction in patient mortality when ICP monitoring was combined with $PtiO_2$ vs ICP alone, with no difference in neurological outcome [33]. Randomized studies have not demonstrated the benefit of $PtiO_2$, so its use is based on expert opinion. [22,35–37]

Furthermore, these studies evaluating the relationship between $PtiO_2$ and cerebral perfusion pressure (CPP) only involve a small number of patients. [10]

We hypothesize that at equal $PaCO_2$, PaO_2 and hemoglobin there is a linear relationship between CPP and $PtiO_2$ and therefore $PtiO_2$ is a direct reflection of cerebral blood flow.

The aim of this work is to analyze the relationship between $PtiO_2$ and CPP and the impact of $PtiO_2$ on the outcome of severe traumatic brain injury patients to optimize the management of secondary brain injury and improve neurological outcome.

2 Material and methods

2.1 Study design

This is a single-center retrospective cohort study evaluating cerebral hemodynamics in severe head injury patients admitted to the neurosurgical intensive care unit at Lille University Hospital. Patients must have had intracranial monitoring by ICP and $PtiO_2$.

2.2 Patients

We included adult patients hospitalized in the neurosurgical intensive care unit at Lille University Hospital with severe trauma brain injury and receiving intracranial monitoring between 1 April 2016 and 30 March 2023.

2.3 Data

The data were collected by extracting data from the ICCA® Phillips software, studying the neurosurgical resuscitation file, the surgical discharge file and the emergency unit file.

The analysis of the data includes elements retrieved from entry into the unit up to 5 days of care.

2.3.1 Data on general characteristics

The general characteristics studied were age, sex, Glasgow Coma Scale at initial management, simplified severity index (IGS II) and Charlson Comorbidity Index.

2.3.2 Data on neuroradiological characteristics

The radiological characteristics are the nature of the initial lesions assessed on the CT scan and initial cerebral MRI if performed. These include cerebral contusion, subarachnoid hemorrhage (SAH), intraventricular hemorrhage (IVH), subdural hematomas (SDH), extradural hematomas (EDH) and diffuse axonal injury (DAI).

The location of the $PtiO_2$ probe assessed on a unsystematic brain CT scan. This is located in the pericontusional zone or in a healthy zone, at the discretion of the person who placed it (neurosurgeon or intensivist).

The presence of an external ventricular drainage (EVD) during the management is also collected.

2.3.3 Data on general hemodynamic characteristics

The characteristics relating to general hemodynamics consist of mean arterial pressure (MAP), measured by an arterial catheter in the radial or femoral position, with zero located at the level of the right atrium of the heart. Mean doses of noradrenaline and mean hemoglobin levels. These data were averaged over the first 5 days of care.

2.3.4 Data on cerebral hemodynamic characteristics

The characteristics relating to cerebral hemodynamics consist of cerebral tissue oxygen pressure ($PtiO_2$), cerebral perfusion pressure (CPP), intracranial pressure (ICP), partial oxygen pressure (PaO_2), fraction of inspired oxygen (FiO_2), ratio of PaO_2 to FiO_2, partial carbon dioxide pressure ($PaCO_2$).

$PtiO_2$ is measured using an intra-parenchymal Clark probe at Lille University Hospital. The model used comes from the LICOX® brand (Integra Neurosciences Implants,

France, SAS) associated with a LICOX® monitor (Integra Neurosciences, GMS, Germany), see appendix 4. Calibration is carried out before the probe is inserted.

ICP is measured using a CAMINO® probe (Natus Medical Incorporated, San Diego, USA) with a CAMINO® monitor (Integra Lifesciences, Ireland).

These probes are associated with an insertion catheter that accommodates at least two probes. This is most frequently implanted in the scalp, at the intersection of the mid-pupillary line and the hairline.

This procedure is carried out in the operating theatre or intensive care unit under strict aseptic conditions, by a neurosurgeon or a intensivist. The choice of placement area is at their discretion.

The data are taken into account for the first 5 days of monitoring, due to the absence of possible in vivo calibration of the $PtiO_2$ with drift of the measured values beyond this period.

$PtiO_2$ values above 50 mmHg and from the first 5 hours were removed from the analysis, in order to take this equilibration time into account.

PaO_2 and $PaCO_2$ were measured using arterial blood gas at least once daily for the first 5 days.

The PaO_2/FiO_2 ratio was calculated during the analysis.

These data were averaged over the first 5 days of care.

2.3.5 Data on patient outcomes

Information on the outcome of patients was retrieved from their medical records at least 6 months after their stay in intensive care.

The outcome of the population was assessed using the Glasgow Outcome Scale (GOS), scored from 1 to 5.

We dichotomized the GOS score into "bad outcome" (GOS 1, 2 and 3) and "good outcome" (GOS 4 and 5).

2.4 Statistical analysis

2.4.1 Descriptive analysis

Categorical variables are expressed as frequency and percentage and quantitative variables as means ± standard deviation in case of normal distribution or medians (interquartile range, IQR) otherwise. Normality of distributions was checked graphically and using the Shapiro-Wilk test.

2.4.2 Univariate analysis

Relationship between $PtiO_2$ and CPP was assessed using a Pearson correlation coefficient.

2.4.3 Multivariate analysis

An analysis of covariance model (ANCOVA) was used to assess this relationship after adjustment on predefined confounding factors (age, gender, external ventricular derivation, $PtiO_2$ probe placement area, hemoglobin, noradrenaline, PaO_2/FiO_2 ratio, $PaCO_2$ and types of cerebral lesions). Partial r-squared of CPP was derived from the model.

Relationship between $PtiO_2$ and the GOS (1+2+3 versus 4+5) was assessed using a logistic regression model adjusted on predefined confounding factors (age, gender,

Glasgow coma scale, Simplified Acute Physiology Score, external ventricular drainage, $PtiO_2$ probe placement area, hemoglobin, PaO_2/FiO_2 ratio, $PaCO_2$, types of cerebral lesions and the Charlson Comorbidity Index). Odds ratios were derived from model with their 95% confidence intervals as effect size.

For adjusted analyses, missing values were handled by multiple imputation procedures. Missing data were imputed under the missing at random assumption using a regression switching approach (chained equation with m = 20 imputations) with predictive mean matching method for continuous variables and logistic regression (binary, ordinal, or polynomial) for qualitative variables [38]. The imputation procedure was performed using the main baseline characteristics and outcomes, and estimates obtained in the different imputed data sets were combined using the Rubin's rules [39,40]. For the ANCOVA analysis, the partial r-squared for PPC is the median value (and range) among the imputed datasets.

2.4.4 Significance

Statistical testing was conducted at the two-tailed α-level of 0.05. Data were analyzed using the SAS software version 9.4 (SAS Institute, Cary, NC).

2.4.5 Regulatory framework

The use of the data is supervised by the Data Protection Officer of the GHT Lille Métropole Flandre Intérieur, and is recorded in the data processing register of the Lille University Hospital, see Appendix 3.

The reference methodology is MR-004, so patient consent is not required.

3 Results

3.1 Flowchart

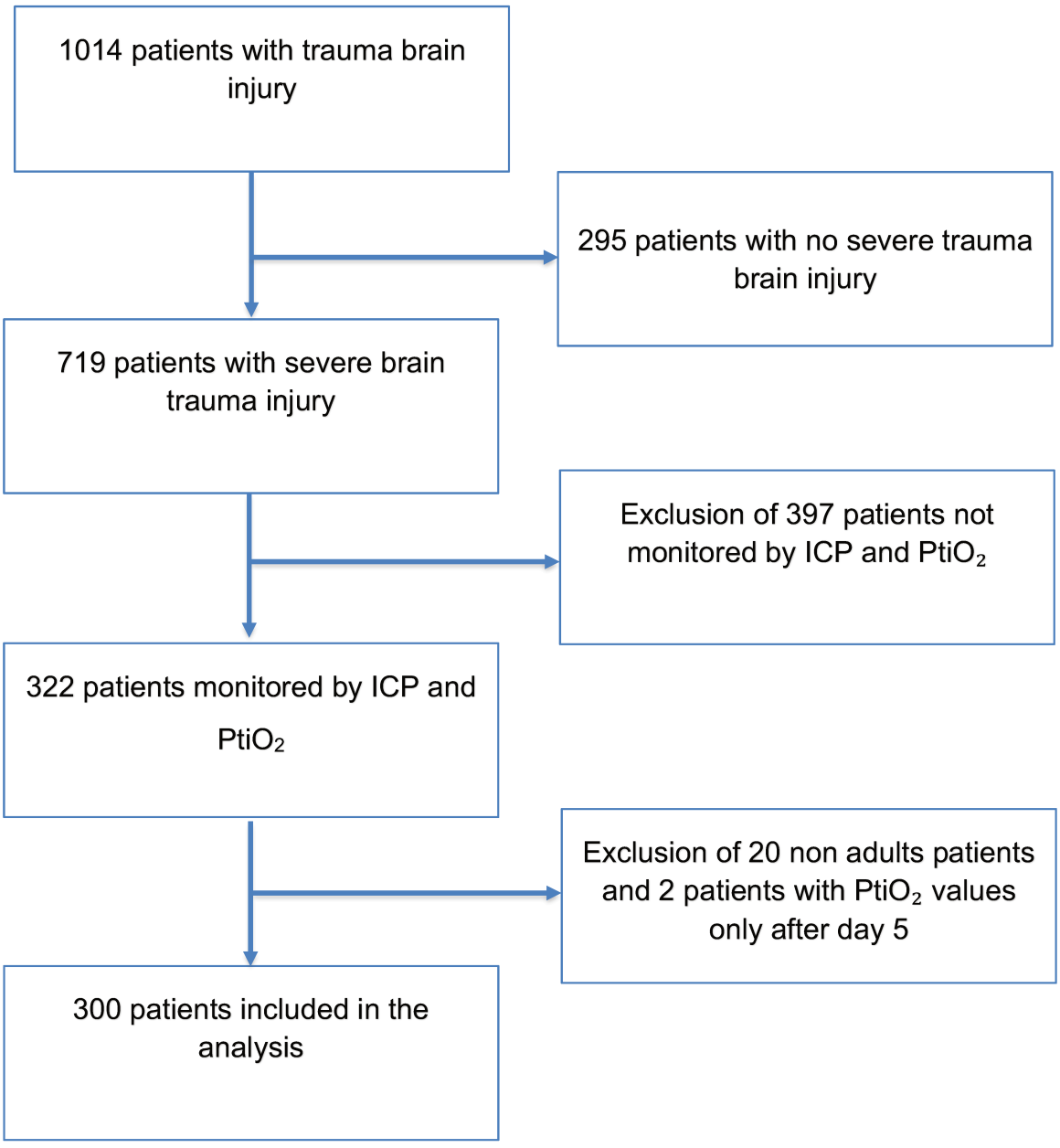

Figure 4 : Flowchart

3.2 Description of patients at inclusion

Variable		
Name	**Unit**	**Population (N = 300)**
Gender Men Women	N (%)	 236 (78,7) 64 (21,3)
Age	Median (Q1 ; Q3)	30 (22 ; 44)
GCS *Missing data*	Median (Q1 ; Q3) *N*	6 (4 ; 8) *1*
IGSII	Median (Q1 ; Q3)	45 (38 ; 50)
CCI	Median (Q1 ; Q3)	0 (0 ; 0)
Primary lesions DAI SDH SAH EDH IVH Cerebral contusion	N (%)	 104 (34,7) 167 (55,7) 203 (67,7) 73 (24,3) 75 (25) 239 (79,9)
$PtiO_2$ zone Healthy Pericontusional	N (%)	 119 (39,7) 181 (60,3)
EVD	N (%)	12 (4)
MAP	Median (Q1 ; Q3) in mmHg	94 (89 ; 99)
Noradrenaline	Median (Q1 ; Q3) in mg/h	1.0 (0.6 ; 1.5)
Hemoglobin *Missing data*	Median (Q1 ; Q3) in g/dL	10.0 (9.0 ; 12.0) *2*
$PtiO_2$	Median (Q1 ; Q3) in mmHg	25 (21 ; 30)
CPP	Median (Q1 ; Q3) in mmHg	84 (79 ; 88)

ICP	Median (Q1 ; Q3) in mmHg	10 (7 ; 14)
PaO_2	Median (Q1 ; Q3) in mmHg	123 (109 ; 137)
FiO_2 *Missing data*	Median (Q1 ; Q3) in mmHg *N*	0.3 (0.3 ; 0.4) *63*
PaO_2 / FiO_2 *Missing data*	Median (Q1 ; Q3) *N*	363 (281 ; 457) *63*
$PaCO_2$	Median (Q1 ; Q3) in mmHg	37 (35 ; 39)
GOS 1 2 3 4 5 1+2+3 4+5 *Missing data*	N (%) N	 40 (13,8) 5 (1,7) 50 (17,2) 98 (33,8) 97 (33,4) 95 (32,8) 195 (67,2) *10*

Table 1 : General description

3.3 Association between $PtiO_2$ and CPP

3.3.1 Univariate analysis between $PtiO_2$ and CPP

In univariate analysis, there is a relationship between $PtiO_2$ and CPP with a Pearson correlation coefficient of 0.16 and a p-value of 0.006. Figure 4 shows the scatterplot of $PtiO_2$ as a function of CPP.

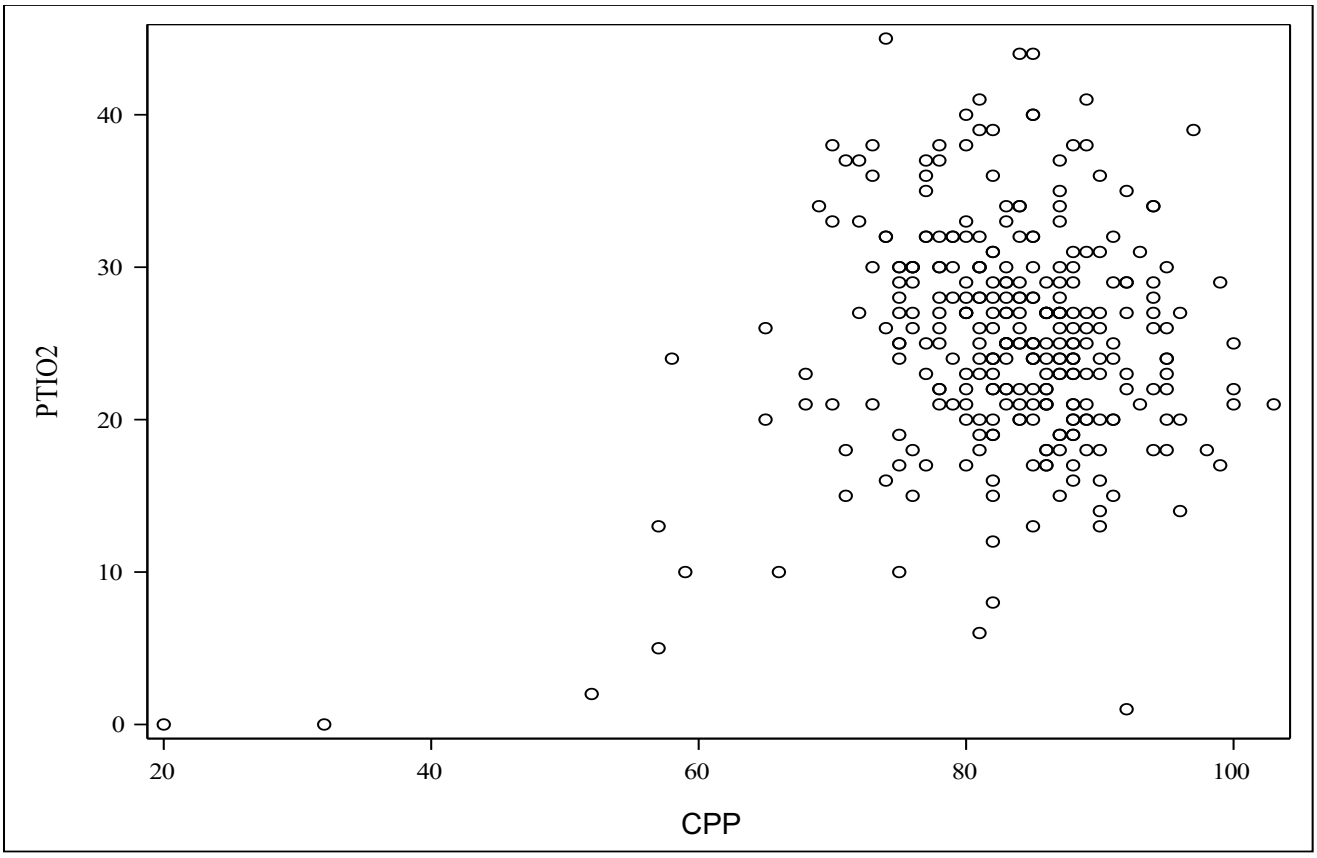

Figure 5 : Representation of the $PtiO_2$ and CPP relationship in univariate analysis.

3.3.2 Relationship between $PtiO_2$ and CPP adjusted for confounding factors

3.3.2.1 After multiple imputation

Variable	Effect Estimate	95% CI	P-value
CPP	0,14	[0,05 ; 0,23]	0,0018
Age	-0.12	[-0,18 ; -0,05]	0.0003
Gender	-1,17	[-3,21 ; 0,87]	0,26
EVD	-0.35	[-4,50 ; 3,79]	0.87
EDH	0,62	[-1,32 ; 2,56]	0,53
IVH	-0.35	[-2.23 ; 1.54]	0.72

SAH	0,77	[-1.03 ; 2.58]	0,40
SDH	-0,75	[-2,44 ; 0,95]	0,39
DAI	-0,29	[-2,06 ; 1,49]	0,75
Cerebral contusion	-0,75	[-2,83 ; 1,34]	0,48
Injured area $PtiO_2$	0,24	[-1,45 ; 1,92]	0,78
Noradrenaline	-0,41	[-1,49 ; 0,66]	0,45
$PaCO_2$	0,09	[-0,19 ; 0,37]	0,52
PaO_2/FiO_2	0,0006	[-0,007 ; 0,008]	0,87
Hemoglobin	0.94	[0,41 ; 1,48]	0.0005

Table 2 : Relationship between $PtiO_2$ and CPP adjusted for confounding factors after multiple imputation.

The partial R^2 of CPP on this model shows a median variance of 0.033 [0.032; 0.034].

3.3.2.2 On complete cases

The total number of complete cases was 234.

Variable	Effect estimate	95% CI	Squared partial corr type II	P-value
CPP	0,06	[-0,06 ; 0,18]	0,005	0,32
Age	-0,10	[-0,17 ; -0,03]	0,035	0,005
Gender	-0,83	[-3,08 ; 1,43]	0,002	0,47
EVD	-0 ,64	[-4,71 ; 3,44]	0,0004	0,76
EDH	1,23	[-0,93 ; 3,38]	0,006	0,26
IVH	1,07	[-2,23 ; 2,00]	0,00005	0,91
SAH	0,54	[-1,43 ; 2,51]	0,001	0,59
SDH	0,28	[-1,57 ; 2,14]	0,0004	0,76
DAI	-0,66	[-2,61 ; 1,30]	0,002	0,51

Cerebral contusion	-0,09	[-2,33 ; 2,14]	0,00003	0,93
Injured area $PtiO_2$	-0,12	[-1,94 ; 1,71]	0,00007	0,90
Noradrenaline	-0,58	[-1,71 ; 0,56]	0,005	0,32
$PaCO_2$	0,05	[-0,25 ; 0,34]	0,0004	0,76
PaO_2/FiO_2	0,0006	[-0,007 ; 0,008]	0,0001	0,88
Hemoglobin	1,13	[0,54 ; 1,71]	0,06	0,0002

Table 3 : Relationship between $PtiO_2$ and CPP adjusted for confounding factors on complete cases.

3.4 Impact of $PtiO_2$ on GOS score adjusted for confounding factors.

3.4.1.1 After multiple imputation

Variable	OR	95% CI	P-value
$PtiO_2$	1,06	[1,02 ; 1,11]	0,0037
Age	0,96	[0,96 ; 1,01]	0,31
Gender	1,06	[0,52 ; 2,16]	0,87
CCI	1,05	[0,70 ; 1,57]	0,81
GCS	1,08	[0,97 ; 1,20]	0,15
Hemoglobin	0,86	[0,73 ; 1,07]	0,21
IGSII	0,97	[0,94 ; 1,00]	0,053
EDH	1,04	[0,50 ; 2,16]	0,92
IVH	0,73	[0,38 ; 1,39]	0,34
SAH	0,70	[0,37 ; 1,32]	0,27
SDH	0,92	[0,51 ; 1,64]	0,78
DAI	0,37	[0,20 ; 0,68]	0,0014

Cerebral contusion	0,75	[0,35 ; 1,60]	0,46
EVD	0,10	[0,02 ; 0,48]	0,0039
Injured area $PtiO_2$	0,95	[0,53 ; 1,70]	0,86
$PaCO_2$	1,05	[0,96 ; 1,16]	0,29
PaO_2/FiO_2	1,00	[0,99 ; 1,00]	0,29

Table 4 : Multivariate analysis of the impact of $PtiO_2$ on the GOS score after multiple imputation.

Figure 5 shows the relationship between $PtiO_2$ and neurological outcome represented by the GOS.

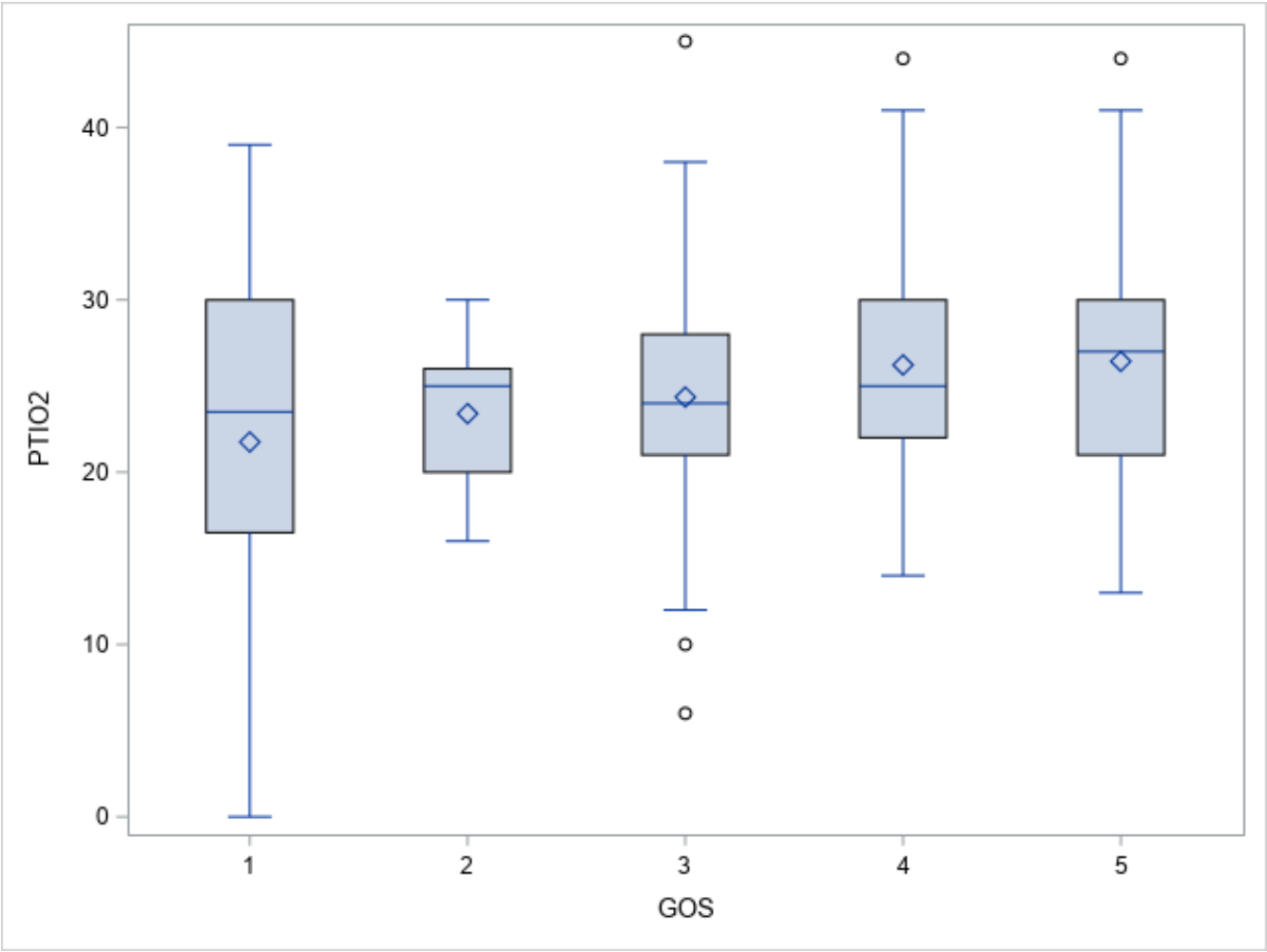

Figure 6 : Relationship between $PtiO_2$ and GOS.

3.4.1.2 *On complete cases*

The total number of complete cases was 223.

Variable	OR	95% CI	P-value
$PtiO_2$	1,05	[1,00 ; 1,11]	0,043
Age	0,99	[0,96 ; 1,02]	0,50
Gender	0,91	[0,40 ; 2,01]	0,82
CCI	1,054	[0,68 ; 1,64]	0,82
GCS	1,00	[0,88 ; 1,14]	0,95
Hemoglobin	0,98	[0,79 ; 1,22]	0,84
IGSII	0,97	[0,94 ; 1,01]	0,10
EDH	0,97	[0,42 ; 2,24]	0,94
IVH	0,74	[0,348 ; 1,57]	0,43
SAH	0,58	[0,28 ; 1,37]	0,14
SDH	0,70	[0,35 ; 1,37]	0,29
DAI	0,30	[0,15 ; 0,61]	0,0009
Cerebral contusion	0,77	[0,34 ; 1,74]	0,53
EVD	0,11	[0,02 ; 0,53]	0,005
Injured area $PtiO_2$	1,07	[0,56 ; 2,05]	0,84
$PaCO_2$	1,00	[0,90 ; 1,11]	0,99
PaO_2/FiO_2	1,00	[1,00 ; 1,01]	0,18

Table 5 : Multivariate analysis of the impact of $PtiO_2$ on the GOS on complete cases.

4 Discussion

4.1 Discussion of the results

We found a statistically significant relationship between CPP and $PtiO_2$ in both unadjusted and adjusted analysis, except in the whole-case analysis.

Our study population is similar to recent epidemiological data on head trauma. It consisted of young men with no medical history [2]. The mechanism of head trauma was not documented in our study.

An increase in cerebral perfusion pressure seems discretely associated with better cerebral oxygenation, measured by $PtiO_2$. This effect is small, suggesting the involvement of other factors in the measurement of $PtiO_2$.

Hemoglobin has a positive and statistically significant effect on $PtiO_2$, so a 1 g/dL increase in hemoglobin would increase $PtiO_2$ by 1 mmHg.

Conversely, age has a significantly negative effect on $PtiO_2$. An increase in age of one year, is associated with a decrease in $PtiO_2$ of 0.12 mmHg.

These results, although statistically significant, are weak and of little relevance in clinical practice. Nevertheless, they are consistent with the Canadian CAHR-TBI cohort [41], which found a correlation between $PtiO_2$ and CPP. Other studies also highlight an increase in $PtiO_2$ by increasing CPP. [26,42]

Thus, there appears to be a relationship between $PtiO_2$ and CPP. Other factors seem to influence $PtiO_2$ apart from CPP such as age or hemoglobin according to our results.

It has been described in the literature that the presence of cerebral hypoxia is multifactorial and may occur independently of preserved CPP [12,28] .

These results are consistent with an American retrospective study, although their population was small, older and had a higher mortality rate. [43]

Our CPP and $PtiO_2$ values are above the standards set by international recommendations [18]. However, a retrospective New Zealand study shows that cerebral oxygenation decreases in patients with intracranial hypertension with a ICP > 40 mmHg for one hour [44] . Thus, there could be a negative correlation between high ICP and low $PtiO_2$ in patients with severe and prolonged intracranial hypertension.

In our population, the median hemoglobin of patients was 10 g/dL, above the recommended figures [18], hemoglobin being a factor influencing $PtiO_2$. In a retrospective analysis, a decrease in $PtiO_2$ was found when hemoglobin was less than 9 g/dL, associated with a poorer neurological outcome [45,46]. In addition, a randomized prospective study showed an improvement in $PtiO_2$ after transfusion of packed red blood cells. [47]

Although the PaO_2 is not significant in our population, a retrospective study highlights that a minimum PaO_2 threshold should be higher than that presented in the SIBICC recommendations, making it possible to avoid being at the ischemic threshold, by monitoring of a "BOx ratio" $PtiO_2/PaO_2$.[48]

It therefore seems worthwhile to monitor ICP, in conjunction with $PtiO_2$, in order to detect ischemic episodes. A 2005 study reported that up to 30% of monitored patients developed secondary cerebral ischemia, as assessed by $PtiO_2$. [49]

$PtiO_2$ represents a balance between oxygen delivery and consumption [50]. As it is measured directly in the cerebral parenchyma, it nevertheless remains complex and focal. Interpretation of $PtiO_2$ is tricky and depends on external factors such as the area where the probe is placed in a healthy or pericontusional zone.

In our population, the $PtiO_2$ probe is placed in the pericontusional zone in 60% of cases, which may underestimate the relationship, considering that injured areas are less well oxygenated. [22]

Our population showed a high survival rate of 86.2%, in contrast to the literature, which shows a mortality rate of between 20 and 40% for similar general characteristics [31,32,51,52]. In our population, these results are associated with a good neurological outcome in 67.2% of patients.

These results can be explained by the way in which TBI patients are admitted to the shock trauma center. Only patients with a good chance of survival are admitted to the unit.

We highlight a positive and significant impact of $PtiO_2$ on the GOS. A one unit increase in $PtiO_2$ is associated with a 6.4% increase in the chance of a favorable neurological outcome.

Our analysis shows a significant negative effect of the presence of an EVD and the presence of DAI on the GOS score.

These results are consistent with the literature. Observational studies [28,30,49] and a review of the literature [32] have highlighted the fact that a drop in $PtiO_2$ results in an unfavorable neurological outcome. The BOOST-II feasibility study, the first randomized study to investigate the use of $PtiO_2$, intends that monitoring $PtiO_2$ would lead to better cerebral oxygenation, associated with a better neurological outcome. [35]

Diffuse axonal injury are associated with poorer neurological outcome, through degeneration and persistent inflammation of the white matter [53–55]. Furthermore, it is possible that all the patients in our study had DAI not seen on the initial brain CT

scan, but that those whose DAI was described by the radiologist were initially more severe patients.

The presence of an EVD and its impact on outcome are biased by the severity of this population. The shunt is fitted in situations of refractory intracranial hypertension, in a category of patients with a poorer neurological outcome. There are few data on the relationship between the presence of an EVD and neurological outcome, but these are in favor of a reduction in the GOS and an increase in mortality. [56,57]

The outcome of patients is not only correlated to their neurological condition, but also to other comorbidities caused by the polytrauma, which may explain a higher rate of death or major sequelae following hospitalization.

4.2 Discussion of the method

This was a single-center retrospective study. The study was carried out in a center with expertise in neurocritical care, which led to a center effect and selection bias, and was specific to the Lille University Hospital. Patients were initially admitted to the shock trauma center before being transferred to the neurosurgical intensive care unit. This means that the most serious patients, whose prognosis and initial clinical condition are considered to be poor, are not systematically included in the neurocritical care population. This may explain the high survival rate, particularly with a good neurological outcome.

One of the strong points of this study is that it includes a large number of patients who benefited from ICP and $PtiO_2$ monitoring, which is rarely found in the literature concerning this topic.

There was little missing data for most variables.

Analysis showed that perfusion pressures and cerebral oxygenation were in line with international recommendations [18], with a good outcome.

After their stay in intensive care, these patients receive dedicated care. The patient's pathway is mapped out in a specialized rehabilitation center, followed by follow-up in the region's trauma brain injury network.

Another limitation is that management is not standardized, and remains at the discretion of the intensivist and neurosurgeon, particularly as regards the indications for surgery and the type of monitoring used. Patients judged to be less serious could be monitored solely by an ICP sensor.

We studied a $PtiO_2$ value averaged over the first five days for each patient; however, it is above all the absolute value, the duration of exposure, and therefore the cumulative total ischemia, that could impact the outcome of patients. [35,58]

Assessment of the $PtiO_2$ probe placement zone is dichotomized into healthy zone or pericontusional zone according to brain CT scan. In this population, 60% of $PtiO_2$ probes are located in the pericontusional zone. However, a normal CT scan appearance does not rule out a location in a contused or pericontusional zone.

There are no clear recommendations on the exact position of the $PtiO_2$ probe, although one publication recommends its position in the pericontusional zone. [59]

The exact role of $PtiO_2$ in clinical practice remains to be demonstrated in high-powered studies such as BOOST-3 or BONANZA, the results of which are expected [12,60], although the French multicenter prospective study OXY-TC is negative. [36]

Severe head trauma is a complex pathology with a phenotypic expression specific to each patient. In view of this, an individualized approach using multimodal monitoring seems essential.

Technical and scientific developments in this area may enable us to overcome these problems, coupled with the use of algorithms based on PRx or ORx [61,62] . The same applies to the monitoring of metabolic crises using the lactate/pyruvate ratio by cerebral micro-dialysis. The latter, when altered, has been shown to result in excess mortality . [63,64]

5 Conclusion

This study shows us that there is a weak positive relationship between $PtiO_2$ and CPP and that a better $PtiO_2$ is associated with a better neurological outcome.

$PtiO_2$ would be an important and independent component of multimodal monitoring of severe head injury.

Invasive cerebral monitoring seems to be the rule in order to optimize cerebral macrocirculation and microcirculation, as well as metabolism, requiring individualized therapeutic strategies to be defined and validated. [22]

The provision of rehabilitation care as part of cranial trauma patient networks could be an area for development in the future.

Conclusion en Français

Cette étude nous montre qu'il existerait une relation positive faible linéaire entre la $PtiO_2$ et la PPC et qu'une meilleure $PtiO_2$ est associée à un meilleur devenir neurologique.

La $PtiO_2$ serait un élément important et indépendant du monitorage multimodal du traumatisé crânien grave.

Le monitorage cérébral invasif semble être la règle afin d'optimiser la macro et la micro circulation cérébrale, ainsi que le métabolisme, nécessitant des stratégies thérapeutiques individualisées à définir et valider. [22]

La prise en charge en rééducation dans le cadre de réseaux de patients traumatisés crâniens pourrait être un axe à développer dans le futur.

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Références

[1] Geeraerts T, Velly L, Abdennour L, Asehnoune K, Audibert G, Bouzat P, et al. Management of severe traumatic brain injury (first 24hours). Anaesth Crit Care Pain Med 2018;37:171–86. https://doi.org/10.1016/j.accpm.2017.12.001.

[2] Brazinova A, Rehorcikova V, Taylor MS, Buckova V, Majdan M, Psota M, et al. Epidemiology of Traumatic Brain Injury in Europe: A Living Systematic Review. J Neurotrauma 2021;38:1411–40. https://doi.org/10.1089/neu.2015.4126.

[3] Taylor CA, Bell JM, Breiding MJ, Xu L. Traumatic Brain Injury-Related Emergency Department Visits, Hospitalizations, and Deaths - United States, 2007 and 2013. Morb Mortal Wkly Rep Surveill Summ Wash DC 2002 2017;66:1–16. https://doi.org/10.15585/mmwr.ss6609a1.

[4] Santé Publique France. Epidémiologie des traumatismes crâniens en France et dans les pays occidentaux 2019.

[5] Haitsma IK, Maas AIR. Advanced monitoring in the intensive care unit: brain tissue oxygen tension. Curr Opin Crit Care 2002;8:115–20. https://doi.org/10.1097/00075198-200204000-00005.

[6] Taran S, Pelosi P, Robba C. Optimizing oxygen delivery to the injured brain. Curr Opin Crit Care 2022;28:145–56. https://doi.org/10.1097/MCC.0000000000000913.

[7] Lindblad C, Raj R, Zeiler FA, Thelin EP. Current state of high-fidelity multimodal monitoring in traumatic brain injury. Acta Neurochir (Wien) 2022;164:3091–100. https://doi.org/10.1007/s00701-022-05383-8.

[8] Treggiari MM, Schutz N, Yanez ND, Romand J-A. Role of intracranial pressure values and patterns in predicting outcome in traumatic brain injury: a systematic review. Neurocrit Care 2007;6:104–12. https://doi.org/10.1007/s12028-007-0012-1.

[9] Tran-Dinh A, Depret F, Vigué B. Pression tissulaire cérébrale en oxygène : mieux que la PIC ? n.d.

[10] Lang EW, Czosnyka M, Mehdorn HM. Tissue oxygen reactivity and cerebral autoregulation after severe traumatic brain injury*. Crit Care Med 2003;31:267.

[11] Casault C, Couillard P, Kromm J, Rosenthal E, Kramer A, Brindley P. Multimodal brain monitoring following traumatic brain injury: A primer for intensive care practitioners. J Intensive Care Soc 2022;23:191–202. https://doi.org/10.1177/1751143720980273.

[12] Bernard F, Barsan W, Diaz-Arrastia R, Merck LH, Yeatts S, Shutter LA. Brain Oxygen Optimization in Severe Traumatic Brain Injury (BOOST-3): a multicentre, randomised, blinded-endpoint, comparative effectiveness study of brain tissue oxygen and intracranial pressure monitoring versus intracranial pressure alone. BMJ Open 2022;12:e060188. https://doi.org/10.1136/bmjopen-2021-060188.

[13] Czosnyka M, Smielewski P, Kirkpatrick P, Menon DK, Pickard JD. Monitoring of Cerebral Autoregulation in Head-Injured Patients. Stroke 1996;27:1829–34. https://doi.org/10.1161/01.STR.27.10.1829.

[14] Jaeger M, Dengl M, Meixensberger J, Schuhmann MU. Effects of cerebrovascular pressure reactivity-guided optimization of cerebral perfusion pressure on brain tissue

oxygenation after traumatic brain injury. Crit Care Med 2010;38:1343–7. https://doi.org/10.1097/CCM.0b013e3181d45530.

[15] Chesnut RM, Temkin N, Carney N, Dikmen S, Rondina C, Videtta W, et al. A trial of intracranial-pressure monitoring in traumatic brain injury. N Engl J Med 2012;367:2471–81. https://doi.org/10.1056/NEJMoa1207363.

[16] Diaz-Arrastia R, Kochanek PM, Bergold P, Kenney K, Marx CE, Grimes ColJB, et al. Pharmacotherapy of Traumatic Brain Injury: State of the Science and the Road Forward: Report of the Department of Defense Neurotrauma Pharmacology Workgroup. J Neurotrauma 2014;31:135–58. https://doi.org/10.1089/neu.2013.3019.

[17] Murray GD, Butcher I, McHugh GS, Lu J, Mushkudiani NA, Maas AIR, et al. Multivariable Prognostic Analysis in Traumatic Brain Injury: Results from The IMPACT Study. J Neurotrauma 2007;24:329–37. https://doi.org/10.1089/neu.2006.0035.

[18] Chesnut R, Aguilera S, Buki A, Bulger E, Citerio G, Cooper DJ, et al. A management algorithm for adult patients with both brain oxygen and intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). Intensive Care Med 2020;46:919–29. https://doi.org/10.1007/s00134-019-05900-x.

[19] Stocchetti N, Maas AIR. Traumatic Intracranial Hypertension. N Engl J Med 2014;370:2121–30. https://doi.org/10.1056/NEJMra1208708.

[20] Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GWJ, Bell MJ, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. Neurosurgery 2017;80:6–15. https://doi.org/10.1227/NEU.0000000000001432.

[21] Tavakoli S, Peitz G, Ares W, Hafeez S, Grandhi R. Complications of invasive intracranial pressure monitoring devices in neurocritical care 2017. https://doi.org/10.3171/2017.8.FOCUS17450.

[22] Leach MR, Shutter LA. How much oxygen for the injured brain – Can invasive parenchymal catheters help? Curr Opin Crit Care 2021;27:95–102. https://doi.org/10.1097/MCC.0000000000000810.

[23] Mulvey JM, Dorsch NWC, Mudaliar Y, Lang EW. Multimodality Monitoring in Severe Traumatic Brain Injury: The Role of Brain Tissue Oxygenation Monitoring. Neurocrit Care 2004;1:391–402. https://doi.org/10.1385/NCC:1:3:391.

[24] Al Barajraji M, Bogossian E, Dewitte O, Gaspard N, El Hadwe S, Minini A, et al. Safety profile of an intracranial multimodal monitoring bolt system for neurocritical care: a single-center experience. Acta Neurochir (Wien) 2021;163:3259–66. https://doi.org/10.1007/s00701-021-04992-z.

[25] Longhi L, Pagan F, Valeriani V, Magnoni S, Zanier ER, Conte V, et al. Monitoring brain tissue oxygen tension in brain-injured patients reveals hypoxic episodes in normal-appearing and in peri-focal tissue. Intensive Care Med 2007;33:2136–42. https://doi.org/10.1007/s00134-007-0845-2.

[26] Johnston AJ, Steiner LA, Coles JP, Chatfield DA, Fryer TD, Smielewski P, et al. Effect of cerebral perfusion pressure augmentation on regional oxygenation and metabolism after head injury. Crit Care Med 2005;33:189–95; discussion 255-257. https://doi.org/10.1097/01.ccm.0000149837.09225.bd.

[27] Marín-Caballos AJ, Murillo-Cabezas F, Cayuela-Domínguez A, Domínguez-Roldán JM, Rincón-Ferrari MD, Valencia-Anguita J, et al. Cerebral perfusion pressure and risk of brain hypoxia in severe head injury: a prospective observational study. Crit Care 2005;9:R670–6.

https://doi.org/10.1186/cc3822.

[28] Chang JJJ, Youn TS, Benson D, Mattick H, Andrade N, Harper CR, et al. Physiologic and functional outcome correlates of brain tissue hypoxia in traumatic brain injury. Crit Care Med 2009;37:283–90. https://doi.org/10.1097/CCM.0b013e318192fbd7.

[29] Oddo M, Levine JM, Mackenzie L, Frangos S, Feihl F, Kasner SE, et al. Brain hypoxia is associated with short-term outcome after severe traumatic brain injury independently of intracranial hypertension and low cerebral perfusion pressure. Neurosurgery 2011;69:1037–45; discussion 1045. https://doi.org/10.1227/NEU.0b013e3182287ca7.

[30] Spiotta AM, Stiefel MF, Gracias VH, Garuffe AM, Kofke WA, Maloney-Wilensky E, et al. Brain tissue oxygen-directed management and outcome in patients with severe traumatic brain injury. J Neurosurg 2010;113:571–80. https://doi.org/10.3171/2010.1.JNS09506.

[31] Narotam PK, Morrison JF, Nathoo N. Brain tissue oxygen monitoring in traumatic brain injury and major trauma: outcome analysis of a brain tissue oxygen-directed therapy. J Neurosurg 2009;111:672–82. https://doi.org/10.3171/2009.4.JNS081150.

[32] Maloney-Wilensky E, Gracias V, Itkin A, Hoffman K, Bloom S, Yang W, et al. Brain tissue oxygen and outcome after severe traumatic brain injury: a systematic review. Crit Care Med 2009;37:2057–63. https://doi.org/10.1097/CCM.0b013e3181a009f8.

[33] Hoffman H, Abi-Aad K, Bunch KM, Beutler T, Otite FO, Chin LS. Outcomes associated with brain tissue oxygen monitoring in patients with severe traumatic brain injury undergoing intracranial pressure monitoring 2021. https://doi.org/10.3171/2020.11.JNS203739.

[34] Bouzat P, Marques-Vidal P, Zerlauth J-B, Sala N, Suys T, Schoettker P, et al. Accuracy of brain multimodal monitoring to detect cerebral hypoperfusion after traumatic brain injury*. Crit Care Med 2015;43:445–52. https://doi.org/10.1097/CCM.0000000000000720.

[35] Okonkwo DO, Shutter LA, Moore C, Temkin NR, Puccio AM, Madden CJ, et al. Brain Oxygen Optimization in Severe Traumatic Brain Injury Phase-II: A Phase II Randomized Trial. Crit Care Med 2017;45:1907–14. https://doi.org/10.1097/CCM.0000000000002619.

[36] Payen J-F, Richard M, Francony G, Audibert G, Barbier EL, Bruder N, et al. Comparison of strategies for monitoring and treating patients at the early phase of severe traumatic brain injury: the multicentre randomised controlled OXY-TC trial study protocol. BMJ Open 2020;10:e040550. https://doi.org/10.1136/bmjopen-2020-040550.

[37] Payen J-F, Launey Y, Chabanne R, Gay S, Francony G, Gergele L, et al. Intracranial pressure monitoring with and without brain tissue oxygen pressure monitoring for severe traumatic brain injury in France (OXY-TC): an open-label, randomised controlled superiority trial. Lancet Neurol 2023;22:1005–14. https://doi.org/10.1016/S1474-4422(23)00290-9.

[38] (PDF) MICE: Multivariate Imputation by Chained Equations in R. ResearchGate 2024. https://doi.org/10.18637/jss.v045.i03.

[39] Rubin DB. 1988: AN OVERVIEW OF MULTIPLE IMPUTATION n.d.

[40] Meng X-L, Rubin DB. Performing likelihood ratio tests with multiply-imputed data sets. Biometrika 1992;79:103–11. https://doi.org/10.1093/biomet/79.1.103.

[41] Gomez A, Sekhon M, Griesdale D, Froese L, Yang E, Thelin EP, et al. Cerebrovascular pressure reactivity and brain tissue oxygen monitoring provide complementary information regarding the lower and upper limits of cerebral blood flow control in traumatic brain injury: a CAnadian High Resolution-TBI (CAHR-TBI) cohort study. Intensive Care Med Exp 2022;10:54. https://doi.org/10.1186/s40635-022-00482-3.

[42] Johnston AJ, Steiner LA, Chatfield DA, Coles JP, Hutchinson PJ, Al-Rawi PG, et al. Effect of cerebral perfusion pressure augmentation with dopamine and norepinephrine on global and focal brain oxygenation after traumatic brain injury. Intensive Care Med 2004;30:791–7. https://doi.org/10.1007/s00134-003-2155-7.

[43] Eriksson EA, Barletta JF, Figueroa BE, Bonnell BW, Vanderkolk WE, McAllen KJ, et al. Cerebral perfusion pressure and intracranial pressure are not surrogates for brain tissue oxygenation in traumatic brain injury. Clin Neurophysiol Off J Int Fed Clin Neurophysiol 2012;123:1255–60. https://doi.org/10.1016/j.clinph.2011.08.035.

[44] Donnelly J, Smielewski P, Adams H, Zeiler FA, Cardim D, Liu X, et al. Observations on the Cerebral Effects of Refractory Intracranial Hypertension After Severe Traumatic Brain Injury. Neurocrit Care 2020;32:437–47. https://doi.org/10.1007/s12028-019-00748-x.

[45] Oddo M, Levine JM, Kumar M, Iglesias K, Frangos S, Maloney-Wilensky E, et al. Anemia and brain oxygen after severe traumatic brain injury. Intensive Care Med 2012;38:1497–504. https://doi.org/10.1007/s00134-012-2593-1.

[46] Sekhon MS, McLean N, Henderson WR, Chittock DR, Griesdale DEG. Association of hemoglobin concentration and mortality in critically ill patients with severe traumatic brain injury. Crit Care Lond Engl 2012;16:R128. https://doi.org/10.1186/cc11431.

[47] Zygun DA, Nortje J, Hutchinson PJ, Timofeev I, Menon DK, Gupta AK. The effect of red blood cell transfusion on cerebral oxygenation and metabolism after severe traumatic brain injury. Crit Care Med 2009;37:1074–8. https://doi.org/10.1097/CCM.0b013e318194ad22.

[48] Dellazizzo L, Demers S-P, Charbonney E, Williams V, Serri K, Albert M, et al. Minimal PaO_2 threshold after traumatic brain injury and clinical utility of a novel brain oxygenation ratio. J Neurosurg 2019;131:1639–47. https://doi.org/10.3171/2018.5.JNS18651.

[49] Stiefel MF, Spiotta A, Gracias VH, Garuffe AM, Guillamondegui O, Maloney-Wilensky E, et al. Reduced mortality rate in patients with severe traumatic brain injury treated with brain tissue oxygen monitoring. J Neurosurg 2005;103:805–11. https://doi.org/10.3171/jns.2005.103.5.0805.

[50] Rosenthal G, Hemphill JC, Sorani M, Martin C, Morabito D, Obrist WD, et al. Brain tissue oxygen tension is more indicative of oxygen diffusion than oxygen delivery and metabolism in patients with traumatic brain injury. Crit Care Med 2008;36:1917–24. https://doi.org/10.1097/CCM.0b013e3181743d77.

[51] Paget. Trauma centre admissions for traumatic brain injury in France: One-year epidemiological analysis of prospectively collected data - ScienceDirect n.d. https://www-sciencedirect-com.ressources-electroniques.univ-lille.fr/science/article/pii/S2352556821000072?via%3Dihub (accessed February 7, 2025).

[52] Green JA, Pellegrini DC, Vanderkolk WE, Figueroa BE, Eriksson EA. Goal Directed Brain Tissue Oxygen Monitoring Versus Conventional Management in Traumatic Brain Injury: An Analysis of In Hospital Recovery. Neurocrit Care 2013;18:20–5. https://doi.org/10.1007/s12028-012-9797-7.

[53] Johnson VE, Stewart JE, Begbie FD, Trojanowski JQ, Smith DH, Stewart W. Inflammation and white matter degeneration persist for years after a single traumatic brain injury. Brain J Neurol 2013;136:28–42. https://doi.org/10.1093/brain/aws322.

[54] Javeed F, Rehman L, Afzal A, Abbas A. Outcome of diffuse axonal injury in moderate and severe traumatic brain injury. Surg Neurol Int 2021;12:384. https://doi.org/10.25259/SNI_573_2020.

[55] Ravikanth R, Majumdar P. Prognostic Significance of Magnetic Resonance Imaging in Detecting Diffuse Axonal Injuries: Analysis of Outcomes and Review of Literature. Neurol India 2022;70:2371–7. https://doi.org/10.4103/0028-3886.364066.

[56] Bales JW, Bonow RH, Buckley RT, Barber J, Temkin N, Chesnut RM. Primary External Ventricular Drainage Catheter Versus Intraparenchymal ICP Monitoring: Outcome Analysis. Neurocrit Care 2019;31:11–21. https://doi.org/10.1007/s12028-019-00712-9.

[57] Chau CYC, Craven CL, Rubiano AM, Adams H, Tülü S, Czosnyka M, et al. The Evolution of the Role of External Ventricular Drainage in Traumatic Brain Injury. J Clin Med 2019;8:1422. https://doi.org/10.3390/jcm8091422.

[58] van den Brink WA, van Santbrink H, Steyerberg EW, Avezaat CJ, Suazo JA, Hogesteeger C, et al. Brain oxygen tension in severe head injury. Neurosurgery 2000;46:868–76; discussion 876-878. https://doi.org/10.1097/00006123-200004000-00018.

[59] Robba C, Taccone FS, Citerio G. Monitoring cerebral oxygenation in acute brain-injured patients. Intensive Care Med 2022;48:1463–6. https://doi.org/10.1007/s00134-022-06788-w.

[60] ACTRN12619001328167. The BONANZA trial- a randomised controlled trial that is testing whether a management strategy guided by early brain tissue oxygen monitoring in patients in with severe traumatic brain injury improves long term neurological and functional outcomes | Cochrane Library n.d. https://doi.org/10.1002/central/CN-02064812.

[61] Lazaridis C, Andrews CM. Brain tissue oxygenation, lactate-pyruvate ratio, and cerebrovascular pressure reactivity monitoring in severe traumatic brain injury: systematic review and viewpoint. Neurocrit Care 2014;21:345–55. https://doi.org/10.1007/s12028-014-0007-7.

[62] Jaeger M, Lang EW. Cerebrovascular pressure reactivity and cerebral oxygen regulation after severe head injury. Neurocrit Care 2013;19:69–73. https://doi.org/10.1007/s12028-013-9857-7.

[63] Marini CP, Stoller C, McNelis J, Del Deo V, Prabhakaran K, Petrone P. Correlation of brain flow variables and metabolic crisis: a prospective study in patients with severe traumatic brain injury. Eur J Trauma Emerg Surg Off Publ Eur Trauma Soc 2022;48:537–44. https://doi.org/10.1007/s00068-020-01447-5.

[64] Timofeev I, Carpenter KLH, Nortje J, Al-Rawi PG, O'Connell MT, Czosnyka M, et al. Cerebral extracellular chemistry and outcome following traumatic brain injury: a microdialysis study of 223 patients. Brain J Neurol 2011;134:484–94. https://doi.org/10.1093/brain/awq353.

[65] Brennan PM, Whittingham C, Sinha VD, Teasdale G. Assessment of level of consciousness using Glasgow Coma Scale tools. BMJ 2024;384:e077538. https://doi.org/10.1136/bmj-2023-077538.

[66] (PDF) Neurological outcome after cardiac arrest: A prospective study of the predictive ability of prognostic biomarkers neuron-specific enolase, glial fibrillary acidic protein, S-100B, and procalcitonin. ResearchGate 2024. https://doi.org/10.3906/sag-1503-64.

Annexe 1

GLASGOW COMA SCALE : Do it this way

GCS EYES VERBAL MOTOR

Institute of Neurological Sciences NHS Greater Glasgow and Clyde

CHECK	OBSERVE	STIMULATE	RATE
For factors Interfering with communication, ability to respond and other injuries	Eye opening , content of speech and movements of right and left sides	Sound: spoken or shouted request Physical: Pressure on finger tip, trapezius or supraorbital notch	Assign according to highest response observed

Eye opening

Criterion	Observed	Rating	Score
Open before stimulus	✔	Spontaneous	4
After spoken or shouted request	✔	To sound	3
After finger tip stimulus	✔	To pressure	2
No opening at any time, no interfering factor	✔	None	1
Closed by local factor	✔	Non testable	NT

Verbal response

Criterion	Observed	Rating	Score
Correctly gives name, place and date	✔	Orientated	5
Not orientated but communication coherently	✔	Confused	4
Intelligible single words	✔	Words	3
Only moans / groans	✔	Sounds	2
No audible response, no interfering factor	✔	None	1
Factor interferring with communication	✔	Non testable	NT

Best motor response

Criterion	Observed	Rating	Score
Obey 2-part request	✔	Obeys commands	6
Brings hand above clavicle to stimulus on head neck	✔	Localising	5
Bends arm at elbow rapidly but features not predominantly abnormal	✔	Normal flexion	4
Bends arm at elbow, features clearly predominantly abnormal	✔	Abnormal flexion	3
Extends arm at elbow	✔	Extension	2
No movement in arms / legs, no interfering factor	✔	None	1
Paralysed or other limiting factor	✔	Non testable	NT

Sites For Physical Stimulation

Finger tip pressure | Trapezius Pinch | Supraorbital notch

Features of Flexion Responses

Modified with permission from Van Der Naalt 2004
Ned Tijdschr Geneeskd

Abnormal Flexion
Slow Sterotyped
Arm across chest
Forearm rotates
Thumb clenched
Leg extends

Normal flexion
Rapid
Variable
Arm away from body

For further information and video demonstration visit www.glasgowcomascale.org

Annexe 1 : Score de Glasgow, d'après [65]

Annexe 2

Score	Functional status	Description
1	Good recovery	Returned to the original functional level and employment with no deficit
2	Moderate disability	Minor neurological deficit that does not interfere with daily functioning or work
3	Severe disability	Significant neurological deficit that interferes with daily activities or prevents return to employment
4	Persistent vegetative state	Coma or severe deficit rendering the patient totally dependent
5	Death	Self-explanatory

Annexe 2 : Score de GOS, d'après [66]

Annexe 3

DIRECTION GENERALE

DEPARTEMENT DES RESSOURCES NUMERIQUES

N/Réf : **DEC24-161**

BOUZIDI Anthony
Délégué à la protection des données

CALMELET Louise
Adjointe au Délégué à la protection des données

Secrétariat Direction des Ressources Numérique
Tél. 03.20.44.44.26
Fax : 03.20.44.58.59

Attestation de déclaration d'un traitement informatique

L'équipe Déléguée à la Protection des Données du GHT Lille Métropole Flandre intérieure atteste que le fichier de traitement ayant pour finalité **: Relation entre pression de perfusion cérébrale et oxygénation cérébrale chez le patient traumatisé crânien grave et impact sur le devenir** mis en œuvre en **2024**, a bien été déclaré par Christophe Huz.

La déclaration est intégrée dans le registre des traitements du Centre Hospitalier Régional Universitaire de Lille.

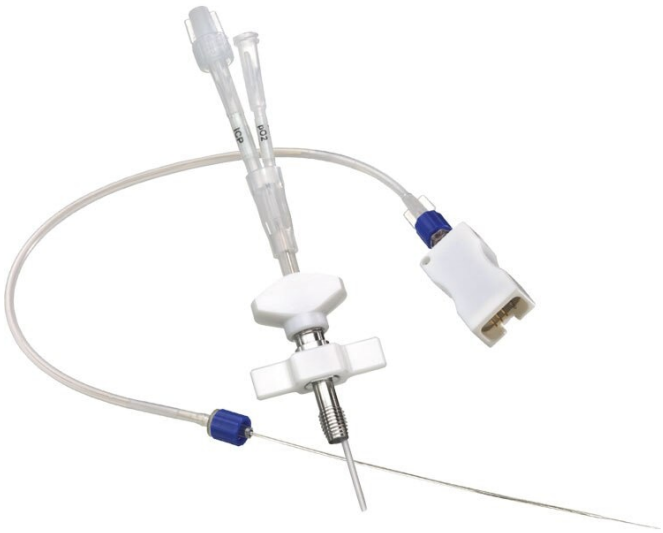
Attestation réalisée pour valoir ce que de droit.

Fait à LILLE, le **01/07/2024**

Le Délégué à la protection des données
BOUZIDI Anthony
Son adjointe
CALMELET Louise

Toute correspondance devra être adressée à :
CHRU de Lille
Département Ressources Numériques
ex Clinique Fontan - 2ème étage – rue du Professeur Laguesse
59037 LILLE Cedex

Annexe 4



Annexe 4 : Capteur et moniteur de $PtiO_2$ Licox® Integra

AUTEUR : Nom : GESTIN **Prénom :** Guillaume

Date de Soutenance : 30 Avril 2025

Titre de la Thèse : Relation entre pression de perfusion cérébrale et oxygénation cérébrale chez le patient traumatisé crânien grave et impact sur le devenir

Thèse - Médecine - Lille 2025

Cadre de classement : Anesthésie-réanimation

DES + FST ou option : Anesthésie-Réanimation

Mots-clés : Traumatisme crânien grave, monitorage hémodynamique cérébral, $PtiO_2$, pression de perfusion cérébrale

Résumé :

Contexte : Le traumatisme crânien grave comporte un taux de mortalité et des séquelles neurologiques importantes. Sa prise en charge est discutée dans la littérature et repose sur l'optimisation de l'oxygénation et de la circulation sanguine cérébrale via un monitorage de l'hémodynamique intra-cérébrale par PIC et $PtiO_2$.

Notre étude vise à évaluer s'il existe une relation linéaire entre la PPC et la $PtiO_2$ et donc que la $PtiO_2$ serait un reflet direct du débit sanguin cérébral, ainsi que l'impact de la $PtiO_2$ sur le devenir des patients.

Matériel et Méthodes : Tous les patients traumatisés crâniens graves hospitalisés en réanimation neurochirurgicale, monitorés par PIC et $PtiO_2$ entre le 1er Avril 2016 et le 30 Mars 2023 ont été sélectionnés. Toutes les données ont été recueillies à l'aide des dossiers patients informatisés.

Résultats : 300 patients ont été inclus. L'analyse univariée entre PPC et $PtiO_2$ retrouve une relation linéaire (Pearson = 0,16, p = 0,006). L'effet observé est similaire en analyse multivariée (effet estimé = 0,14, IC 95% = [0.05 , 0.23] ; p = 0,0018).
Nous retrouvons qu'une meilleure $PtiO_2$ est associée à un meilleur devenir neurologique (OR = 1,06, IC 95% [1.02,1.11], p = 0,0037).

Conclusion : Il existerait une relation positive faible linéaire entre la $PtiO_2$ et la PPC. Une $PtiO_2$ élevée serait associée à un meilleur devenir neurologique et serait un élément important et indépendant du monitorage multimodal du traumatisé crânien grave.

Le monitorage cérébral invasif semble être la règle afin d'optimiser la macro et la micro circulation cérébrale, ainsi que le métabolisme, nécessitant des stratégies thérapeutiques individualisées à valider par des études de meilleurs niveaux de preuve.

Composition du Jury :

Président : Monsieur le Professeur Benoît TAVERNIER

Assesseurs : Monsieur le Docteur Marc BARONCINI
Madame le Docteur Natalie DE SA

Directeur : Monsieur le Docteur Christophe HUZ