



Clinical Evidence Intracranial Pressure Monitoring, ICP Burden and Pressure Time Dose

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Effects of Intracranial Pressure Monitoring on Mortality in Patients with Severe Traumatic Brain Injury: A Meta-Analysis

Liang Shen, Zhuo Wang, Zhongzhou Su, Sheng Qiu, Jie Xu, Yue Zhou, Ai Yan, Rui Yin, Bin Lu, Xiaohu Nie, Shufa Zhao, Renfu Yan

Abstract

Background: The Brain Trauma Foundation (BTF) guidelines published in 2007 suggest some indications for intracranial pressure (ICP) monitoring in severe traumatic brain injury (TBI). However, some studies had not shown clinical benefit in patients with severe TBI; several studies had even reported that ICP monitoring was associated with an increased mortality rate. The effect of ICP monitoring has remained controversial, regardless of the ICP monitoring guidelines. Here we performed a meta-analysis of published studies to assess the effects of ICP monitoring in patients with severe TBI.

Methods: We searched three comprehensive databases, the Cochrane Library, PUBMED, and EMBASE, for studies without limitations published up to September 2015. Mortality, ICU LOS, and hospital LOS were analyzed with Review Manager software according to data from the included studies.

Results: Eighteen eligible studies involving 25229 patients with severe TBI were included in our meta-analysis. The results indicated no significant reduction in the ICP monitored group in mortality (hospitalized before 2007), hospital mortality (hospitalized before 2007), mortality in randomized controlled trials. However, overall mortality, mortality (hospitalized after 2007), hospital mortality (hospitalized after 2007), mortality in observational studies (hospitalized after 2007), 2-week mortality, 6-month mortality, were reduced in ICP monitored group. Patients with an increased ICP were more likely to require ICP monitoring.

Source: Shen L, Wang Z, Su Z, Qiu S, Xu J, Zhou Y, et al. (2016) Effects of Intracranial Pressure Monitoring on Mortality in Patients with Severe Traumatic Brain Injury: A Meta-Analysis. PLoS ONE 11(12): e0168901. doi:10.1371/journal.pone.0168901

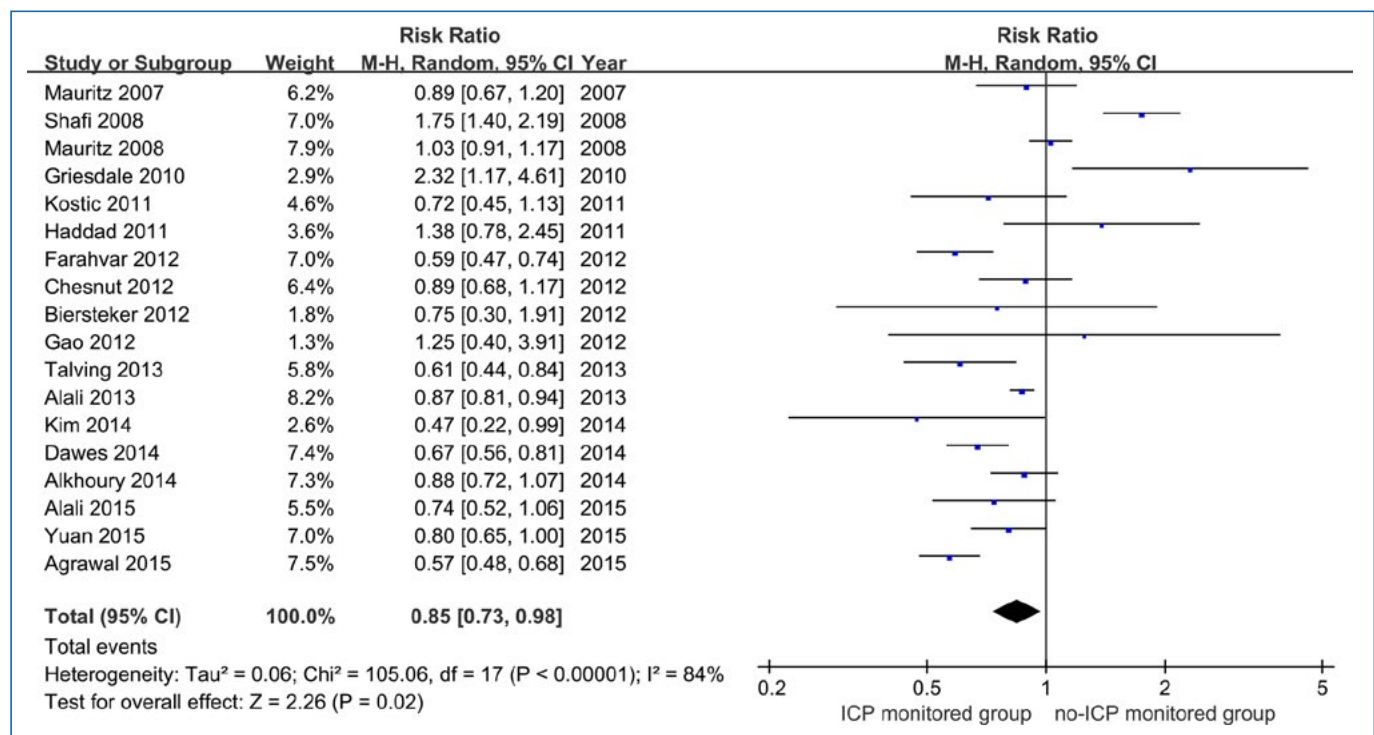


Fig 2: Effect of ICP monitoring on overall mortality among patients with severe TBI.

Visualizing the pressure and time burden of intracranial hypertension in adult and paediatric traumatic brain injury

Güiza F, Depreitere B, Piper I, Citerio G, Chambers I, Jones PA, Lo TY, Enblad P, Nillson P, Feyen B, Jorens P, Maas A, Schuhmann MU, Donald R, Moss L, Van den Berghe G, Meyfroidt G.

Abstract

Purpose: To assess the impact of the duration and intensity of episodes of increased intracranial pressure on 6-month neurological outcome in adult and paediatric traumatic brain injury.

Methods: Analysis of prospectively collected minute-by-minute intracranial pressure and mean arterial blood pressure data of 261 adult and 99 paediatric traumatic brain injury patients from multiple European centres. The relationship of episodes of elevated intracranial pressure (defined as a pressure above a certain threshold during a certain time) with 6-month Glasgow Outcome Scale was visualized in a colour-coded plot.

Results: The colour-coded plot illustrates the intuitive concept that episodes of higher intracranial pressure can only be tolerated for shorter durations: the curve that delineates the duration and intensity of those intracranial pressure episodes associated with worse outcome is an approximately exponential decay curve. In children, the curve resembles that of adults, but the delineation between episodes associated with worse outcome occurs at lower intracranial pressure thresholds. Intracranial pressures above 20 mmHg lasting longer than 37 min in adults, and longer than 8 min in children, are associated with worse outcomes. In a multivariate model, together with known baseline risk factors for outcome in severe traumatic brain injury, the cumulative intracranial pressure-time burden is independently associated with mortality. When cerebrovascular autoregulation, assessed with the low-frequency autoregulation index, is impaired, the ability to tolerate elevated intracranial pressures is reduced. When the cerebral perfusion pressure is below 50 mmHg, all intracranial pressure insults, regardless of duration, are associated with worse outcome.

Conclusions: The intracranial pressure-time burden associated with worse outcome is visualised in a colour-coded plot. In children, secondary injury occurs at lower intracranial pressure thresholds as compared to adults. Impaired cerebrovascular autoregulation reduces the ability to tolerate intracranial pressure insults. Thus, 50 mmHg might be the lower acceptable threshold for cerebral perfusion pressure.

Source: Güiza F, Depreitere B, Piper I, Citerio G, Chambers I, Jones PA, Lo TY, Enblad P, Nillson P, Feyen B, Jorens P, Maas A, Schuhmann MU, Donald R, Moss L, Van den Berghe G, Meyfroidt G. Visualizing the pressure and time burden of intracranial hypertension in adult and paediatric traumatic brain injury. *Intensive Care Med.* 2015 Jun;41(6):1067-76. doi: 10.1007/s00134-015-3806-1. Epub 2015 Apr 18. PMID: 25894624.

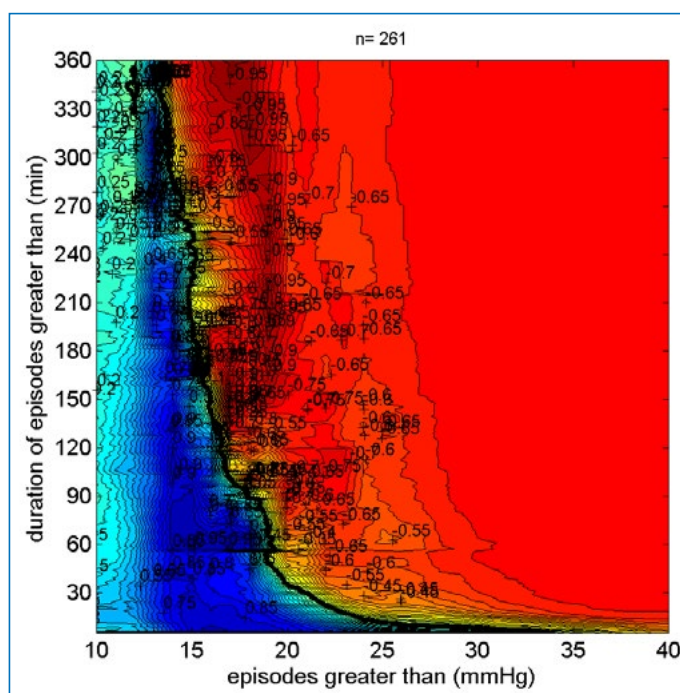


Figure 2 Visualization of correlation between GOS and average number of ICP insults per GOS category. Adult cohort (n = 261). Each colour-coded point in the graph refers to a number of episodes of ICP, defined by a certain ICP intensity threshold (X-axis), and a certain duration threshold (Y-axis). Such an episode is called an ICP insult. The univariate correlation of each type of ICP insult (characterized by ICP intensity and duration thresholds) with outcome is colour coded according to the scale in Fig. 1c. Dark red episodes mean that such ICP insults, on average, are associated with worse outcome (lower GOS categories); dark blue episodes mean that such ICP insults, on average, are associated with better outcome (higher GOS categories). The contour of zero correlation is highlighted in black, and is called the transition curve

Impact of duration and magnitude of raised intracranial pressure on outcome after severe traumatic brain injury: A CENTER-TBI high-resolution group study

Åkerlund CA, Donnelly J, Zeiler FA, Helbok R, Holst A, Cabeleira M, Güiza F, Meyfroidt G, Czosnyka M, Smielewski P, Stocchetti N, Ercole A, Nelson DW

Abstract

Background: Magnitude of intracranial pressure (ICP) elevations and their duration have been associated with worse outcomes in patients with traumatic brain injuries (TBI), however published thresholds for injury vary and uncertainty about these levels has received relatively little attention. In this study, we have analyzed high-resolution ICP monitoring data in 227 adult patients in the CENTER-TBI dataset. Our aim was to identify thresholds of ICP intensity and duration associated with worse outcome, and to evaluate the uncertainty in any such thresholds. We present ICP intensity and duration plots to visualize the relationship between ICP events and outcome. We also introduced a novel bootstrap technique to evaluate uncertainty of the equipose line. We found that an intensity threshold of 18 ± 4 mmHg (2 standard deviations) was associated with worse outcomes in this cohort. In contrast, the uncertainty in what duration is associated with harm was larger, and safe durations were found to be population dependent. The pressure and time dose (PTD) was also calculated as area under the curve above thresholds of ICP. A relationship between PTD and mortality could be established, as well as for unfavourable outcome. This relationship remained valid for mortality but not unfavourable outcome after adjusting for IMPACT core variables and maximum therapy intensity level. Importantly, during periods of impaired autoregulation (defined as pressure reactivity index (PRx) > 0.3) ICP events were associated with worse outcomes for nearly all durations and ICP levels in this cohort and there was a stronger relationship between outcome and PTD. Whilst caution should be exercised in ascribing causation in observational analyses, these results suggest intracranial hypertension is poorly tolerated in the presence of impaired autoregulation. ICP level guidelines may need to be revised in the future taking into account cerebrovascular autoregulation status considered jointly with ICP levels.

Source: Åkerlund CA, Donnelly J, Zeiler FA, Helbok R, Holst A, Cabeleira M, Güiza F, Meyfroidt G, Czosnyka M, Smielewski P, Stocchetti N, Ercole A, Nelson DW; CENTER-TBI High Resolution ICU Sub-Study Participants and Investigators. Impact of duration and magnitude of raised intracranial pressure on outcome after severe traumatic brain injury: A CENTER-TBI high-resolution group study. PLoS One. 2020 Dec 14;15(12):e0243427. doi: 10.1371/journal.pone.0243427. PMID: 33315872; PMCID: PMC7735618.

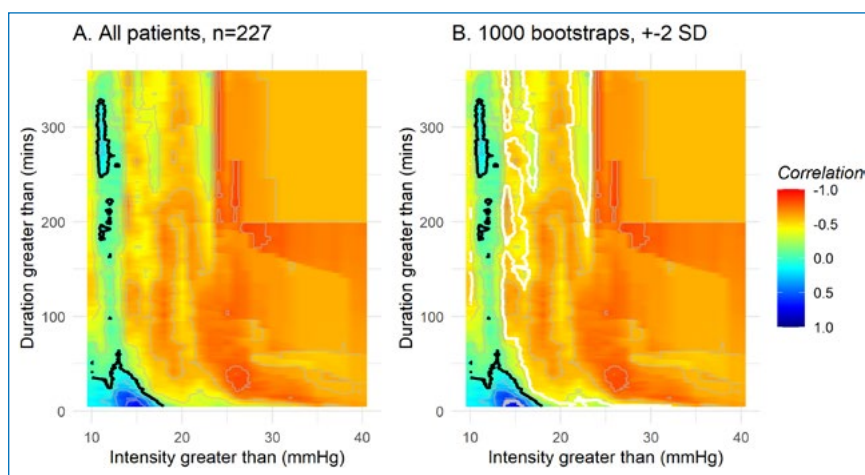


Fig 3. Correlation between number of events above thresholds of intracranial pressure and durations, and outcome (GOS-E score). Red indicates that ICP events are correlated to worse outcome at that specific ICP level and event duration on the map. A. The black line represents the transition line, where there is no correlation between number of events above threshold and outcome. B. The black line represents the mean transition line of 1000 bootstraps. The white lines represent the mean transition line +2 SD, while the grey line represents the mean transition line -2 SD. Above, and to the right, of the white line, there is a high degree of statistical certainty of events being associated with worse outcome, whereas below the grey line, the statistical certainty is high that events are not associated with harm

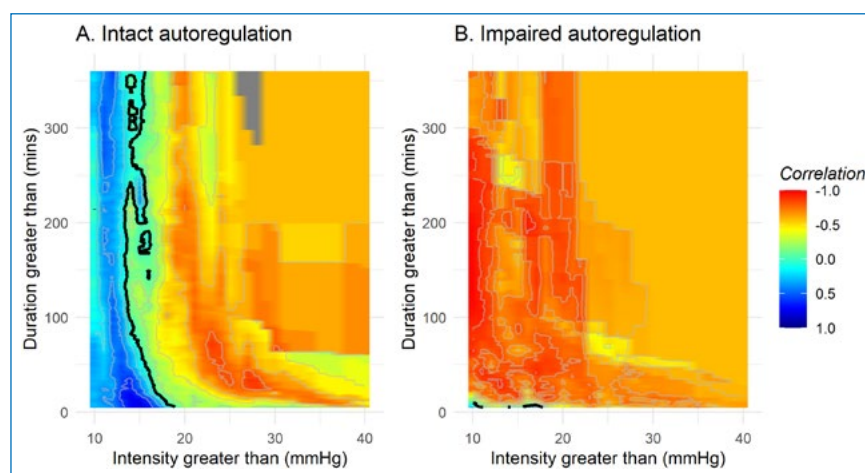


Fig 4. Correlation between number of events above thresholds of intracranial pressure intensity and duration and outcome, stratified by cerebral autoregulatory status. Orange / red areas indicates areas where ICP levels and event durations are associated with worse outcomes. The transition line, i.e. where there is no correlation between number of events and outcome, is drawn in black. All patients contribute some data to both plots, the degree however depending on the extent of their intact vs. impaired autoregulation. A) Intact autoregulation (mean PRx \leq 0.3), B) Impaired autoregulation (mean PRx $>$ 0.3).

Visualising the pressure-time burden of elevated intracranial pressure after severe traumatic brain injury: a retrospective confirmatory study

Donnelly J, Güiza F, Depreitere B, Meyfroidt G, Czosnyka M, Smielewski P

Abstract

Background: Elevated intracranial pressure (ICP) after severe traumatic brain injury (TBI) is an important cause of secondary brain injury, either by hypoperfusion because of decreased cerebral perfusion pressure (CPP), or by mechanical distortion leading to brain herniation. ¹ The thresholds to treat elevated ICP in severe TBI (20 or 22 mm Hg) are based on epidemiological studies, ^{2,3} however, early application of aggressive measures to treat brief episodes of ICP elevations above 20 mm Hg have shown harm. ⁴

Moreover, the association between elevated ICP and outcome is not merely attributable to crossing a threshold, but depends upon the magnitude and the duration of intracranial hypertension. This has been demonstrated in a multicentre prospective European dataset (n=261) by Güiza and colleagues. ⁵

Using a three-dimensional visualisation technique, they showed that worse outcomes (taken at 6 months) could be explained by the interaction between the level of ICP elevation and the duration of the hypertensive episode, confirming a clinically intuitive concept. For instance, insults of high ICP, >30 mm Hg, seemed to be only tolerated for a short time (<8 min), whereas ICP>20 mm Hg leads, on average, to a poor outcome if sustained over 37 min. The ability to tolerate elevated ICP was decreased in children, when cerebrovascular autoregulation was absent, and when CPP was inadequate. To date, this visualisation technique has not been replicated outside of the prospective European dataset. ⁵

Source: Donnelly J, Güiza F, Depreitere B, Meyfroidt G, Czosnyka M, Smielewski P. Visualising the pressure-time burden of elevated intracranial pressure after severe traumatic brain injury: a retrospective confirmatory study. *Br J Anaesth.* 2021 Jan;126(1):e15-e17. doi: 10.1016/j.bja.2020.09.018. Epub 2020 Nov 9. PMID: 33183738.

Critical thresholds of intracranial pressure and cerebral perfusion pressure related to age in paediatric head injury

I R Chambers, P A Jones, T Y M Lo, R J Forsyth, B Fulton, P J D Andrews, A D Mendelow, R A Minns

Abstract

Background: The principal strategy for managing head injury is to reduce the frequency and severity of secondary brain insults from intracranial pressure (ICP) and cerebral perfusion pressure (CPP), and hence improve outcome. Precise critical threshold levels have not been determined in head injured children.

Objective: To create a novel pressure–time index (PTI) measuring both duration and amplitude of insult, and then employ it to determine critical insult thresholds of ICP and CPP in children.

Methods: Prospective, observational, physiologically based study from Edinburgh and Newcastle, using patient monitored blood pressure, ICP, and CPP time series data. The PTI for ICP and CPP for 81 children, using theoretical values derived from physiological norms, was varied systematically to derive critical insult thresholds which delineate Glasgow outcome scale categories.

Results: The PTI for CPP had a very high predictive value for outcome (receiver operating characteristic analyses: area under curve = 0.957 and 0.890 for mortality and favourable outcome, respectively) and was more predictive than for ICP. Initial physiological values most accurately predicted favourable outcome. The CPP critical threshold values determined for children aged 2–6, 7–10, and 11–15 years were 48, 54, and 58 mm Hg, respectively.

Conclusions: The PTI is the first substantive paediatric index of total ICP and CPP following head injury. The insult thresholds generated are identical to age related physiological values. Management guidelines for paediatric head injuries should take account of these CPP thresholds to titrate appropriate pressor therapy.

Sources: Chambers IR, Jones PA, Lo TY, et al. Critical thresholds of intracranial pressure and cerebral perfusion pressure related to age in paediatric head injury. *J Neurol Neurosurg Psychiatry*. 2006;77(2):234–240. doi:10.1136/jnnp.2005.072215

Relationship of “dose” of intracranial hypertension to outcome in severe traumatic brain injury

Vik A, Nag T, Fredriksli OA, Skandsen T, Moen KG, Schirmer-Mikalsen K, Manley GT

Abstract

Object: It has recently been suggested that the degree of intracranial pressure (ICP) above the treatment goal can be estimated by the area under the curve (AUC) of ICP versus time in patients with severe traumatic brain injury (TBI). The objective of this study was to determine whether the calculated “ICP dose”—the ICP AUC—is related to mortality rate, outcome, and Marshall CT classification.

Methods: Of 135 patients (age range 1–82 years) with severe TBI treated during a 5-year period at the authors' institution, 113 patients underwent ICP monitoring (84%). Ninety-three patients with a monitoring time >24 hours were included for analysis of ICP AUC calculated using the trapezoidal method. Computed tomography scans were assessed according to the Marshall TBI classification. Patients with Glasgow Outcome Scale scores at 6 months and >3 years were separated into 2 groups based on outcome.

Results: Sixty patients (65%) had ICP values >20 mm Hg, and 12 (13%) developed severe intracranial hypertension and died secondary to herniation. A multiple regression analysis adjusting for Glasgow Coma Scale score, age, pupillary abnormalities and Injury Severity Scale score demonstrated that the ICP AUC was a significant predictor of poor outcome at 6 months ($p=0.034$) and of death ($p=0.035$). However, it did not predict long-term outcome ($p=0.157$). The ICP AUC was significantly higher in patients with Marshall head injury Categories 3 and 4 (24 patients) than in those with Category 2 (23 patients, $p=0.025$) and Category 5 (46 patients, $p=0.021$) TBIs using the worst CT scan obtained.

Conclusions: The authors found a significant relationship between the dose of ICP, the worst Marshall CT score, and patient outcome, suggesting that the AUC method may be useful in refining and improving the treatment of ICP in patients with TBI.

Source: Vik A, Nag T, Fredriksli OA, Skandsen T, Moen KG, Schirmer-Mikalsen K, Manley GT. Relationship of “dose” of intracranial hypertension to outcome in severe traumatic brain injury. *J Neurosurg.* 2008 Oct;109(4):678–84. doi: 10.3171/JNS/2008/109/10/0678. PMID: 18826355.

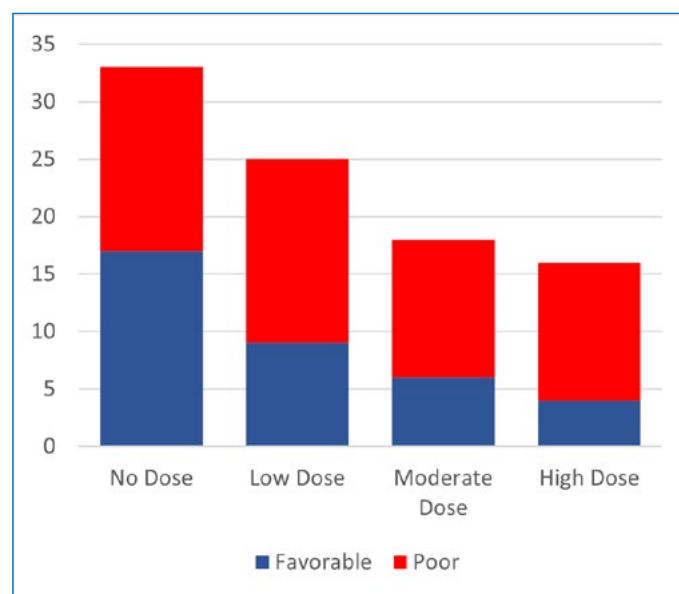


Fig. 3. Graph demonstrating the number of patients with favorable and poor outcomes at 6 months in 4 groups with different doses of ICP AUC: no dose (0 mm Hg*hour), low dose (> 0–75 mm Hg*hour), moderate dose (> 75–200 mm Hg*hour), and high dose (> 200 mm Hg*hour).

Automated measurement of “pressure times time dose” of intracranial hypertension best predicts outcome after severe traumatic brain injury

Kahraman, S., Dutton, R. P., Hu, P., Xiao, Y., Aarabi, B., Stein, D. M., & Scalea, T. M.

Abstract

Background: Earlier, more accurate assessment of secondary brain injury is essential in management of patients with traumatic brain injury (TBI). We assessed the accuracy and utility of high-resolution automated intracranial pressure (ICP) and cerebral perfusion pressure (CPP) recording and their analysis in patients with severe TBI.

Methods: ICP and CPP data for 30 severe TBI patients were collected automatically at 6-second intervals. The degree and duration of ICP and CPP above and below treatment thresholds were calculated as “pressure times time dose” (PTD; mm Hg h) using automated recordings (PTDa) or manual recordings (PTDm) for early stage (trauma resuscitation unit [TRU]) and total monitoring time (TRU and intensive care unit).

Results: Bland-Altman plots showed lack of agreement between PTDa and PTDm. For ICP 20 mm Hg and CPP 60 mm Hg, PTDa, but not PTDm, was significantly higher in patients with unfavorable outcome (Extended Glasgow Outcome Scale score 4) than in patients with favorable outcome (Extended Glasgow Outcome Scale score 4). Total PTDa for ICP 20 mm Hg and CPP 60 mm Hg had high predictive power for functional outcome (area under the receiver operating characteristics curve: 0.92 +/- 0.05 and 0.82 +/- 0.08, respectively) and inhospital mortality (0.76 +/- 0.15 and 0.79 +/- 0.14, respectively) and were strongly correlated with length of intensive care unit stay ($p = 0.009$ and 0.007), length of hospital stay ($p = 0.009$ and 0.005), and discharge Glasgow Coma Scale scores ($p = 0.008$ and $p = 0.038$). PTDa of CPP 100 mm Hg during TRU monitoring and during the first 24 hours showed highest predictive power for mortality (area under the receiver operating characteristics curve: 0.72 +/- 0.18 and 0.85 +/- 0.13, respectively). PTDa was better than PTDm and the duration of episodes alone in predicting outcome.

Conclusions: PTD calculation of high resolution ICP and CPP recording is a reliable and feasible way of monitoring severe TBI patients.

Source: Kahraman S, Dutton RP, Hu P, Xiao Y, Aarabi B, Stein DM, Scalea TM. Automated measurement of "pressure times time dose" of intracranial hypertension best predicts outcome after severe traumatic brain injury. *J Trauma*. 2010 Jul;69(1):110-8. doi: 10.1097/TA.0b013e3181c99853. PMID: 20038855.

Mortality and long-term functional outcome associated with intracranial pressure after traumatic brain injury

Badri S, Chen J, Barber J, Temkin NR, Dikmen SS, Chesnut RM, Deem S, Yanez ND, Treggiari MM

Abstract

Purpose: Elevated intracranial pressure (ICP) has been associated with increased mortality in patients with severe traumatic brain injury (TBI). We have examined whether raised ICP is independently associated with mortality, functional status and neuropsychological functioning in adult TBI patients.

Methods: Data from a randomized trial of 499 participants were secondarily analyzed. The primary endpoints were mortality and a composite measure of functional status and neuropsychological function (memory, speed of information processing, executive function) over a 6-month period. The area under the curve of the ICP profile (average ICP) during the first 48 h of monitoring was the main predictor of interest. Multivariable regression was used to adjust for a priori defined confounders: age, Glasgow Coma Score, Abbreviated Injury Scale-head and hypoxia.

Results: Of the participants, 365 patients had complete 48-h ICP data. The overall 6-month mortality was 18 %. The adjusted odds ratio of mortality comparing 10-mmHg increases in average ICP was 3.12 (95 % confidence interval 1.79, 5.44; $p < 0.01$). Overall, higher average ICP was associated with decreased functional status and neuropsychological functioning ($p < 0.01$). Importantly, among survivors, increasing average ICP was not independently associated with worse performance on neuropsychological testing ($p = 0.46$).

Conclusions: Average ICP in the first 48 h of monitoring was an independent predictor of mortality and of a composite endpoint of functional and neuropsychological outcome at the 6-month follow-up in moderate or severe TBI patients. However, there was no association between average ICP and neuropsychological functioning among survivors.

Source: Badri S, Chen J, Barber J, Temkin NR, Dikmen SS, Chesnut RM, Deem S, Yanez ND, Treggiari MM. Mortality and long-term functional outcome associated with intracranial pressure after traumatic brain injury. *Intensive Care Med.* 2012 Nov;38(11):1800-9. doi: 10.1007/s00134-012-2655-4. Epub 2012 Aug 3. PMID: 23011528.

Intracranial pressure dose and outcome in traumatic brain injury

Sheth KN, Stein DM, Aarabi B, Hu P, Kufera JA, Scalea TM, Hanley DF

Abstract

Objective: Detecting and treating elevated intracranial pressure (ICP) is a cornerstone of management in patients with severe traumatic brain injury. The aim of this study was to determine the association between area under the curve measurement of elevated ICP and clinical outcome.

Methods: Single center observational study using prospectively collected data at a University hospital, level one-trauma center. Sixty prospective patients with severe traumatic brain injury were prospectively enrolled over a 2-year period. Intracranial pressure measurements were captured using a real-time automated, high resolution vital signs data recording system. Mortality and functional outcome were assessed at 30 days, 3 and 6 months using Extended Glasgow Outcome Scale.

Results: Increasing elevated intracranial pressure time dose was associated with mortality (OR 1.08; 95 % confidence interval [CI], 1.01-1.15, $p = 0.03$) and poor functional outcome at 3 (OR 1.04; CI 1.00-1.07, $p = 0.03$) and 6 months (1.04; CI 1.01-1.08, $p = 0.02$). However, there was no association between episodic ICP data and outcome.

Conclusions: These results suggest that pressure time dose measurement of intracranial pressure may be used to predict outcome in severe traumatic brain injury and may be a candidate biomarker in this disease.

Source: Sheth KN, Stein DM, Aarabi B, Hu P, Kufera JA, Scalea TM, Hanley DF. Intracranial pressure dose and outcome in traumatic brain injury. *Neurocrit Care*. 2013 Feb;18(1):26-32. doi: 10.1007/s12028-012-9780-3. PMID: 23055087.

Timing of intracranial hypertension following severe traumatic brain injury

Stein DM, Brenner M, Hu PF, Yang S, Hall EC, Stansbury LG, Menaker J, Scalea TM

Abstract

Background: We asked whether continuous intracranial pressure (ICP) monitoring data could provide objective measures of the degree and timing of intracranial hypertension (ICH) in the first week of neurotrauma critical care and whether such data could be linked to outcome.

Methods: We enrolled adult (>17 years old) patients admitted to our Level I trauma center within 6 h of severe TBI. ICP data were automatically captured and ICP 5-minute means were grouped into 12-hour time periods from admission (hour 0) to >7 days (hour 180). Means, maximum, percent time (% time), and pressure-times-time dose (PTD, mmHg h) of ICP >20 mmHg and >30 mmHg were calculated for each time period.

Results: From 2008 to 2010, we enrolled 191 patients. Only 2.1% had no episodes of ICH. The timing of maximum PTD₂₀ was relatively equally distributed across the 15 time periods. Median ICP, PTD₂₀, %time₂₀, and %time₃₀ were all significantly higher in the 84-180 h time period than the 0-84 h time period. Stratified by functional outcome, those with poor functional outcome had significantly more ICH in hours 84-180. Multivariate analysis revealed that, after 84 h of monitoring, every 5% increase in PTD₂₀ was independently associated with 21% higher odds of having a poor functional outcome (adjusted odds ratio = 1.21, 95% CI 1.02-1.42, p = 0.03).

Conclusions: Although early elevations in ICP occur, ICPs are the highest later in the hospital course than previously understood, and temporal patterns of ICP elevation are associated with functional outcome. Understanding this temporal nature of secondary insults has significant implications for management.

Sources: Stein DM, Brenner M, Hu PF, Yang S, Hall EC, Stansbury LG, Menaker J, Scalea TM. Timing of intracranial hypertension following severe traumatic brain injury. *Neurocrit Care*. 2013 Jun;18(3):332-40. doi: 10.1007/s12028-013-9832-3. PMID: 23494545.

High-resolution intracranial pressure burden and outcome in subarachnoid hemorrhage

Federico Magni, Matteo Pozzi, Matteo Rota, Alessia Vargiolu, Giuseppe Citerio

Abstract

Background: Background and purpose: Intracranial pressure (ICP) control is a therapeutic target in patients with aneurysmal subarachnoid hemorrhage, although only a limited number of studies assessed its course and effect on outcome. Pressure-time dose (PTDICP) is a method to quantify the burden and the time spent above a defined threshold of ICP. PTDICP or its relationship with outcome has never been evaluated in aneurysmal subarachnoid hemorrhage.

Methods: Analysis of data prospectively collected from aneurysmal subarachnoid hemorrhage patients admitted to Neurointensive Care Unit. Monitored data, including intraparenchymal ICP, were digitally recorded minute-by-minute in the first 7 days. PTDICP (mm Hg h) was computed using 4 predefined thresholds (15, 20, 25, and 30 mm Hg). Outcome was assessed through Extended Glasgow Outcome Scale at hospital discharge and at 6 months.

Results: Fifty-five patients were enrolled. Forty-two patients (76%) presented with a poor clinical grade. Overall, mortality was 17% at hospital discharge and 34% at 6 months. Half of patients required extensive therapy to control high ICP during day 1. Median ICP was 10 mm Hg (4-75), whereas median PTDICP₁₅, PTDICP₂₀, PTDICP₂₅, PTDICP₃₀ were, respectively, 13, 4, 2, and 1 mm Hg h. We observed an association between mortality at hospital discharge and higher level of PTDICP using 20, 25, and 30 mm Hg as thresholds and between exposure to a moderate-level PTDICP₃₀ and unfavorable long-term outcome.

Conclusions: PTDICP may better define one of the insults that the brain suffers after aneurysmal rupture, and exposure to moderate PTDICP₃₀ was significant prognostic factor of 6-month unfavorable outcome.

Sources: Magni F, Pozzi M, Rota M, Vargiolu A, Citerio G. High-Resolution Intracranial Pressure Burden and Outcome in Subarachnoid Hemorrhage. *Stroke*. 2015 Sep;46(9):2464-9. doi: 10.1161/STROKEAHA.115.010219. Epub 2015 Aug 4. PMID: 26243224.

Investigation of the Relationship Between the Burden of Raised ICP and the Length of Stay in a Neuro-Intensive Care Unit

Shaw M, Moss L, Hawthorne C, Kinsella J, Piper I

Abstract

Objectives: Raised intracranial pressure (ICP) is well known to be indicative of a poor outcome in traumatic brain injury (TBI). This phenomenon was quantified using a pressure time index (PTI) model of raised ICP burden in a paediatric population. Using the PTI methodology, this pilot study is aimed at investigating the relationship between raised ICP and length of stay (LOS) in adults admitted to a neurological intensive care unit (neuro-ICU).

Materials and methods: In 10 patients admitted to the neuro-ICU following TBI, ICP was measured and data from the first 24 h were analysed. The PTI is a bounded area under the curve, where the bound is the threshold limit of interest for the signal. The upper bound of 20 mmHg for ICP is commonly used in clinical practice. To fully investigate the relationship between ICP and LOS, further bounds from 1 to 40 mmHg were used during the PTI calculations. A backwards step Poisson regression model with a log link function was used to find the important thresholds for the prediction of full LOS, measured in hours, in the neuro-ICU.

Results: The fit was assessed using a Chi-squared deviance goodness of fit method, which showed a non-significant p value of 0.97, indicating a correctly specified model. The backwards step strategy, minimising the model's Akaike information criteria (AIC) at each change, found that levels 13-16, 18 and 20-21 combined were the most predictive. From this model it can be shown that for every 1 mmHg/h increase in burden, as measured by the PTI, the LOS has a base exponential increase of approximately 2 h, with the largest increases in the LOS given at the 20-mmHg threshold level.

Conclusions: This model demonstrates that increased duration of raised ICP in the early monitoring period is associated with a prolonged LOS in the neuro-ICU. Further validation of the PTI model in a larger cohort is currently underway as part of the CHART-ADAPT project. Second, further adjustment with known predictors of outcome, such as severity of injury, would help to improve the fit and validate the current combination of predictors.

Source: Shaw M, Moss L, Hawthorne C, Kinsella J, Piper I. Investigation of the Relationship Between the Burden of Raised ICP and the Length of Stay in a Neuro-Intensive Care Unit. *Acta Neurochir Suppl.* 2018;126:205-208. doi: 10.1007/978-3-319-65798-1_42. PMID: 29492562.

Significance of ICP-related parameters for the treatment and outcome of severe traumatic brain injury

Pan Y, Xue Y, Zhao P, Ding J, Ren Z, Xu J

Abstract

Objective: To analyze the significance of intracranial pressure (ICP)-related parameters on outcome in patients with severe traumatic brain injury. The ICP-related parameters included ICP, ICP dose (DICP), regression of the correlation coefficient between amplitude and pressure (RAP), pressure reactivity index (PRx), and cerebral perfusion pressure (CPP).

Methods: A retrospective analysis was performed using clinical information from 29 patients with severe traumatic brain injury who were admitted to the Department of Neurosurgery from January 2018 to January 2019. All patients underwent ICP probe implantation after admission. Patients were followed up for 6 months after discharge, and were categorized into either the favorable or unfavorable outcome group based on their Glasgow Outcome Scale score. The differences in ICP, DICP, RAP, PRx, and CPP between the two groups were analyzed for their effects on outcome.

Results: The average ICP, DICP, PRx, and RAP values in patients with favorable outcomes were significantly lower than in patients with unfavorable outcomes, while CPP values were significantly higher in the favorable outcome group.

Conclusion: Average ICP, DICP, PRx, RAP, and CPP values may indicate disease status and relate to patient outcomes. It is important to use multiple parameters to predict patients' disease severity and prognosis.

Source: Pan Y, Xue Y, Zhao P, Ding J, Ren Z, Xu J. Significance of ICP-related parameters for the treatment and outcome of severe traumatic brain injury. *J Int Med Res.* 2020 Aug;48(8):300060520941291. doi: 10.1177/0300060520941291. PMID: 32854551; PMCID: PMC7459188.

A management algorithm for patients with intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC)

Hawryluk GWJ, Aguilera S, Buki A, Bulger E, Citerio G, Cooper DJ, Arrastia RD, Diring M, Figaji A, Gao G, Geocadin R, Ghajar J, Harris O, Hoffer A, Hutchinson P, Joseph M, Kitagawa R, Manley G, Mayer S, Menon DK, Meyfroidt G, Michael DB, Oddo M, Okonkwo D, Patel M, Robertson C, Rosenfeld JV, Rubiano AM, Sahuquillo J, Servadei F, Shutter L, Stein D, Stocchetti N, Taccone FS, Timmons S, Tsai E, Ullman JS, Vespa P, Videtta W, Wright DW, Zammit C, Chesnut RM

Abstract

Background: Management algorithms for adult severe traumatic brain injury (sTBI) were omitted in later editions of the Brain Trauma Foundation's sTBI Management Guidelines, as they were not evidence-based.

Methods: We used a Delphi-method-based consensus approach to address management of sTBI patients undergoing intracranial pressure (ICP) monitoring. Forty-two experienced, clinically active sTBI specialists from six continents comprised the panel. Eight surveys iterated queries and comments. An in-person meeting included whole- and small-group discussions and blinded voting. Consensus required 80% agreement. We developed heatmaps based on a traffic-light model where panelists' decision tendencies were the focus of recommendations.

Results: We provide comprehensive algorithms for ICP-monitor-based adult sTBI management. Consensus established 18 interventions as fundamental and ten treatments not to be used. We provide a three-tier algorithm for treating elevated ICP. Treatments within a tier are considered empirically equivalent. Higher tiers involve higher risk therapies. Tiers 1, 2, and 3 include 10, 4, and 3 interventions, respectively. We include inter-tier considerations, and recommendations for critical neuroworsening to assist the recognition and treatment of declining patients. Novel elements include guidance for autoregulation-based ICP treatment based on MAP Challenge results, and two heatmaps to guide (1) ICP-monitor removal and (2) consideration of sedation holidays for neurological examination.

Conclusions: Our modern and comprehensive sTBI-management protocol is designed to assist clinicians managing sTBI patients monitored with ICP-monitors alone. Consensus-based (class III evidence), it provides management recommendations based on combined expert opinion. It reflects neither a standard-of-care nor a substitute for thoughtful individualized management.

Source: Hawryluk GWJ, Aguilera S, Buki A, Bulger E, Citerio G, Cooper DJ, Arrastia RD, Diring M, Figaji A, Gao G, Geocadin R, Ghajar J, Harris O, Hoffer A, Hutchinson P, Joseph M, Kitagawa R, Manley G, Mayer S, Menon DK, Meyfroidt G, Michael DB, Oddo M, Okonkwo D, Patel M, Robertson C, Rosenfeld JV, Rubiano AM, Sahuquillo J, Servadei F, Shutter L, Stein D, Stocchetti N, Taccone FS, Timmons S, Tsai E, Ullman JS, Vespa P, Videtta W, Wright DW, Zammit C, Chesnut RM. A management algorithm for patients with intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). *Intensive Care Med.* 2019 Dec;45(12):1783-1794. doi: 10.1007/s00134-019-05805-9. Epub 2019 Oct 28. PMID: 31659383; PMCID: PMC6863785.

Intracranial Pressure Time Dose (ImPETO)

Giuseppe Citerio (principal investigator)

Study Description

Intracranial pressure (ICP) monitoring is the most common neuromonitoring modality used in neurocritical care (NCCU). Its application both as a stand-alone monitoring or in association with other systems (brain oxygenation, brain microdialysis, electroencephalography, transcranial Doppler ultrasound, etc.) has several indications, which rely on local, national policies, and international guidelines. In 2014, ESICM with the Neurocritical Care Society released a multidisciplinary Consensus Statement to provide a guidance on Multimodality Monitoring in Neurocritical Care, including ICP: "ICP and CPP monitoring are recommended as a part of protocol-driven care in patients who are at risk of elevated intracranial pressure based on clinical and/or imaging features. (Strong recommendation, moderate quality of evidence)". The most recent Brain Trauma Foundation guidelines focused on the importance of ICP monitoring, especially in severe traumatic brain injury, but a living systematic review showed that the compliance rate to these guidelines was low (31%; range 18-83%). Most of the ICP monitoring guidance orbits around traumatic brain injury, while there are uncertainties around indication of ICP monitoring in non-traumatic brain injury (acute subarachnoid hemorrhage and intracerebral hemorrhage).

Similarly, ICP thresholds, threshold-based treatment strategies and their impact on outcome have not been established yet. The interpretation of data on ICP practice has a limited value without some reference to the intensity of therapy directed at control of ICP. The Therapy Intensity Level (TIL) may be a more sensitive measure of the severity of pathophysiology but the effect on outcome of existing differences in practice is unclear.

In most intensive care units, ICP values are summarized hourly in bedside charts by trained nurses, as end-hour ICP, and similar data have been used in large randomized clinical trials testing neuroprotective treatments for TBI patients.

However, several single center studies showed that this manual acquisition method is suboptimal and could miss episodes of high ICP compared to high-resolution, computerized acquisition systems. Computers allow also the computation offline of ICP derived parameters. Vik proposed that the degree of ICP above the treatment threshold can be estimated by the area under the curve (AUC) of ICP versus time in patients with TBI, i.e. the "ICP dose". A significant relationship between the ICP dose, the worst Marshall CT score, and patient outcome exists, suggesting that the AUC method may be useful in refining and improving the treatment of ICP in patients with TBI. Moreover, small cohort studies confirmed this relationship between the dose of ICP and patient outcome, suggesting that the dose of ICP may be useful in refining and improving the treatment of ICP in patients with TBI. In a single centre cohort TBI study, increased ICP dose was associated with mortality and poor functional outcome at 6 months. However, there was no association between episodic ICP data and outcome, proposing this index as candidate "biomarker" of the disease.

Even if the concept is attracting, all these computations have been collected a posteriori and no single ICP monitoring system was able to display the ICP dose continuously, making it useful at the bedside.

The new Integra CereLink ICP monitor integrate the possibility of recording and displaying continuously the AUC (Pressure Time Dose, PTD) and other ICP derived variables and provide the possibility of evaluating the utility of this information at the bedside. It offers the opportunity to test in a standardized way the clinical value of the PTD computation in this setting.

Therefore, the study aims to test clinically if PTD recorded continuously is associated to patients' outcome and to identify a threshold of PTD associated with the transition from good to negative outcomes.

Hypothesis:

- High PTD is associated with worse outcome.
- A threshold of PTD associated with good outcomes (mortality and 6 months outcome) might be identified.
- A better PTD summary report, more closely associated with outcome, will make this parameter useful at the bedside.

Intracranial Pressure Time Dose (IMPETO)

Giuseppe Citerio (principal investigator)

Methods: The study is prospective, observational, international cohort study in centers already using the new Integra CereLink ICP monitor (released in spring 2019).

Treatments and clinical decisions will not be affected by the participation to the protocol that is purely observational.

Potential centers involved are listed in the Addendum.

Each investigator will notify the relevant ethics committee, in compliance with the local legislation and rules. Since patients recruited in this study will not be able to provide an informed consent at the time of recruitment (patient in coma requiring ICP monitoring), the responsible clinical/research staff will act as Consultee and consent eligible patients after discussion with the next-of-kin. At follow-up, patients who have regained capacity will be asked to provide Informed Consent for the acute data and follow-up or deny research participation and request destruction of acute data collected.

Data collection will be web-based. Participating centres will register electronically and collect data via an electronic Case-Report Form (RedCAP) and data will be anonymized locally. The data resides at the University Milano-Bicocca; all procedures will comply with the EU regulation on data protection 2016/679 on the protection of natural persons regarding personal data processing and movement.

A reduced set of demographic characteristics, past medical history information, diagnosis, timeline, clinical presentation of ABl and administered treatments will be extracted from patients' medical records.

ICP high-resolution data will be downloaded from the Integra CereLink ICP monitor:

- mean ICP;
- ICP dose. Centres will collect mortality and GOSE at ICU/hospital discharge and GOSE at 6 months. The GOSE at the End-of-Study will be collected via phone structured interviews to patients and/or family members using a validated questionnaire.

Data accuracy will be verified automatically in the database through validity and consistency checks on relevant variables and, additionally, a trained staff at the University of Milano-Bicocca in Monza will periodically perform checks of completeness and consistency of the information to ensure data quality.

Statistical plan: Descriptive statistics will be used to summarize demographic, clinical features and outcomes. Kaplan-Maier estimates will be used to describe mortality and the Cox model to assess the association with PTD adjusting for potential confounders. The shared frailty joint model will be used to assess the predictiveness of the longitudinal PTD profile on mortality. The logistic model will be used to assess the role of PTD on GOSE dichotomized as poor and good outcome (poor outcome GOSE: 1-4; good outcome GOSE: 5-8). All tests will be two-sided with a significant level of 0.05.

No formal sample size calculation was performed but based on the potentiality of recruitment of the centers involved in the study, we expect to enrol at least 200 patients (with an average of 15 patients per center).

Expected results: The PTD (Pressure Time Dose) recorded by the Integra CereLink ICP monitor is related with outcome. Higher PTD are associated with worse outcomes.

- The max PTD associated with good outcomes will be estimated.
- The Investigators aim to identify the best way of summarizing PDT for clinical use.
- To demonstrate that PTD is a better predictor of outcome compared with end-hour ICP values (standard now)

Source: <https://clinicaltrials.gov/ct2/show/record/NCT04459806?term=IMPETO&draw=2&rank=1>

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