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Original Research Article

Association between the outcome of traumatic brain injury patients and cerebrovascular autoregulation, cerebral perfusion pressure, age, and injury grades

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ABSTRACT

Background and objective: The aim of this study was to explore the association of cerebrovascular autoregulation (CA) and optimal cerebral perfusion pressure (CPP) managing conditions with the outcome of traumatic brain injury (TBI) patients including additional information about the patients' age and grade of diffuse axonal injury (DAI).
Materials and methods: The CA monitoring of 28 TBI patients was performed by using ICM+ software (Cambridge, UK). The CA status estimating pressure reactivity indexes (PRx) and CPP data were processed in order to obtain information on the patient-specific treatment conditions by calculating the optimal CPP.
Results: There was a negative correlation between the Glasgow outcome scale (GOS) score and PRx ($r = -0.448$ at hospital discharge and $r = -0.402$ after 6 months). The estimated threshold value PRx of >0.24 was associated with mortality. The correlation coefficients between the GOS score and the difference CPP-optimal CPP were 0.549 at hospital discharge and 0.484 after 6 months. The threshold value of CPP declination from ΔCPPopt per −6 mmHg was associated with mortality. Poorer outcome was predicted for elderly TBI patients (aged >47 years) and patients having a DAI grade of 3.
Conclusions: The association of the GOS score with CPP, CA impairment conditions, age and diffuse axonal injury (DAI) grade showed that the outcomes of TBI patients were associated with patient-specific CPP management and better outcomes were obtained for younger patients, for patients having lower DAI grade and for patients whose CPP was kept within the range from the optimal CPP to the optimal CPP + 10 mmHg.

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1. Introduction

Although the outcome of patients with traumatic brain injury (TBI) is highly associated with the severity of brain injury and many other factors [1,2], it might be improved by optimizing treatment strategies [3–6]. The main factors influencing the possibility to treat the patient for leading to a better outcome are cerebral perfusion pressure (CPP), cerebrovascular autoregulation (CA), age and brain injury severity. The initial state of a TBI patient is estimated according to the Glasgow coma scale (GCS), which together with other factors (age, pupils, computed tomography [CT] scans, etc.) might provide rough prognosis of the outcome [7,8]. Moreover, such prediction of the patient's outcome based on the initial GCS does not contain the patient's treatment information. The impairment of CA has a strong impact on the outcome of the traumatic brain injury (TBI) patients, therefore, it is essential to know the real-time status of CA [9,10]. The consensus has already been achieved that the cerebral blood flow (CBF) autoregulatory state of TBI patients has to be monitored and the individualized treatment strategy should be re-valuated regularly over the time course of CBF autoregulation status [11,12].

The clinically practical method for continuous CA assessment is to calculate a pressure-reactivity index (PRx) as a moving linear correlation coefficient between the reference arterial blood pressure (ABP) and invasively or non-invasively measured intracranial pressure (ICP) slow waves [13–17]. PRx reflects the ability of cerebral vessels to change the diameter in response to the changes in the ABP, while maintaining a stable cerebral blood flow [13]. It is proved that the PRx increased above the critical thresholds is associated with brain vascular deterioration leading to the fatal outcome [18,19]. Different PRx thresholds for the survival (when the averaged PRx is below 0.2–0.25) and for a favorable outcome (when the averaged PRx is below 0.05) were reported in the recent studies [19,20]. Moreover, PRx can be used as a variable for setting the individual target for optimal CPP management [21,22]. Continuous PRx monitoring might help to identify the optimal CPP under the condition of the strongest cerebrovascular autoregulation. The optimal CPP is determined by plotting PRx against CPP in individual cases (by the moving time window of 3 h or even up to 6 h) and by finding the CPP value or CPP range at which PRx is minimal [22]. Minimal PRx reflects the conditions of intact CA. The patients with greater deviation between their averaged CPP and post hoc assessed optimal CPP have worse outcomes after head trauma [22–24]. However, there are a few limitations of practical usage of PRx and optimal CPP-based treatment strategies:

- Statistically determined PRx thresholds for survival are rough due to the usage of averaged PRx values for threshold calculation. In most cases the real-time monitored PRx values varies considerably above and below determined PRx thresholds, therefore, it complicates patients specific treatment decision making. In recent studies it is shown that time of CA impairment (when PRx >0 or PRx is above specific thresholds of mortality) is also important factor associated with the patients' outcome and should be taken into account during patients' treatment [23,25].
- Determination of the optimal CPP requires more time for more accurate and precise estimation (3–6 h). Therefore, delay in making patient's treatment decision might be critical. The real-time monitored CPP value always varies with the delay respectively to the optimal CPP and the differences between the real-time monitored CPP and the optimal CPP are not investigated enough.
- Additional important factors, as age and brain injury rate, influence the patient's outcome and should be taken into account in choosing patient specific treatment strategies [26,27].

The aim of this study was to explore the influence of the CA impairment and the optimal CPP managing conditions on TBI patients' outcome including additional information about the patient's age and the rate of TBI injury as well as to identify the threshold for the difference between the real-time monitored CPP and the optimal CPP.

2. Materials and methods

A total of 28 severe traumatic brain injury patients in different pathophysiological states were monitored simultaneously by using the ICP monitor (Codman) and the ABP monitor (Datex) at Republican Vilnius University Hospital (Lithuania). The data from the ICP monitor and the ABP monitor were collected and processed by using software ICM+ (Cambridge, UK). This software was used for online real-time calculation of the PRx index as well as for determination of optimal CPP values (Fig. 1). All data were used to perform the post hoc analysis in order to extract additional information and optimize monitoring and real-time algorithms.

The following parameters of the monitored data were calculated:

- PRx was calculated as the moving linear correlation coefficient between the ABP and ICP spontaneous slow waves within a 10-min time window. The real time artifacts were rejected from the ABP and ICP data and only the artifact-free data were used for PRx calculation.
- CPP was calculated as the difference between the mean ABP and ICP values within 10-min time window. The optimal CPP values were calculated by plotting the CPP values vs. PRx values and fitting the U-shaped curve over the plotted points taken from 6 h monitoring window. The minimum point of the U shape was kept as an optimal CPP value. The optimal CPP values were rejected in the cases if the U shape fitting was not reliable.
- The difference between the real-time CPP and the optimal CPP was calculated as $\Delta CPPopt = CPP - CPPopt$.
- The total time in percentage of CA impairment when the PRx value exceeded threshold associated with mortality was calculated for each patient.

The Glasgow outcome scale (GOS) score was determined after hospital discharge (GOS_{HD}) and 6 months (GOS_{6M}). The patients' outcome was described as follows: 1, death; 2, persistent vegetative state; 3, severe disability; 4, moderate disability; and 5, low disability. The outcome was considered