Enhanced visualization of optimal cerebral perfusion pressure over time to support clinical decision making

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Abstract

Objective: Cerebrovascular reactivity can provide a continuously updated individualised target for management of CPP, termed CPPopt.

Data Sources: Here we present a concept method of visualisation of autoregulation based CPPopt using data of 4 severe TBI patients with ICP monitoring.

Conclusions: The visualization method addresses some of the main drawbacks of the original methodology and might bring the potential for its clinical application closer.

Introduction

Current guidelines for management of severe traumatic brain injury (TBI) patients recommend keeping ICP below 20 mmHg and CPP within the range of 50-70 mmHg.[1] Although some success has been achieved, it ignores substantial injury-specific and patient-specific variability.[2] A recent trial showed lack of any important outcome benefits of applying one particular fixed ICP treatment cut-off value.[3] One promising approach supports the idea of individualizing perfusion treatment strategies guided by the state of cerebral autoregulation.[4-6] Cerebrovascular pressure reactivity represents a key element of autoregulation. The pressure reactivity index (PRx) can be determined as the moving correlation coefficient between ABP and ICP.[7] With this approach active cerebrovascular reactions can be assessed by observing the response of cerebral blood volume and subsequently ICP to slow spontaneous changes in ABP.[8] However, minute-by-minute values of PRx vary over time and require averaging to provide meaningful values. Additionally whilst PRx provides a method for assessing autoregulation, it does not, by itself, suggest any particular course of action in patient management.

One useful way of 'averaging' PRx and at the same time providing it with an immediate clinical meaning, is to divide its values into different bins according to corresponding predefined CPP ranges. Plotting mean PRx against associated CPP bins frequently produces a U-shaped curve with both hypoperfusion (low CPP) and hyperperfusion (high CPP) associated with worsened cerebrovascular reactivity.[4, 5] Employing curve fitting the lowest point of the individual autoregulation curve can be marked as the 'optimal' CPP (CPPopt) value,

corresponding to the CPP where individual autoregulation is the most effective. These calculations can be repeated every minute from a chosen time range of past data samples (moving window) thus producing a time-trend of CPPopt that can be plotted alongside of CPP and ICP (Figure 1a). Recently, we have demonstrated that larger deviation of CPP from the automatically calculated CPPopt was associated with worse clinical outcome.[4] However, the CPPopt trend does not fully reflect the character of the PRx-CPP relationship, nor does it capture its dynamic nature. In addition, the CPPopt trends can be fairly 'erratic' (noisy), and may often contain many gaps where the PRx-CPP curves cannot robustly be fitted. These effects are likely to be detrimental to the process of clinical introduction of the autoregulation guided CPP therapy.

In this study we therefore aim to improve the CPPopt methodology by introducing a new visualization method that may provide insight into the complete characteristics of the CPP-PRx relationship, and its temporal evolution.

Materials and Methods

Patients

We present the concepts of the new visualization method using data from four randomly selected severe TBI patients who were admitted to the neurocritical care unit in 2013 and underwent monitoring of ICP as part of the TBI management protocol at the University Medical Center Groningen. The local medical ethics committee waived the need for informed consent. The local TBI protocol aimed at keeping the CPP at approximately 60-70 mmHg and the ICP below 20 mmHg.

Data acquisition

ABP was monitored invasively with an intravascular line connected to a pressure transducer (Baxter Healthcare Corp. CardioVascular Group, Irvine, CA) and zeroed at right atrium level. An intraventricular ICP probe (Raumedic Neurovent, Raumedic AG, Helmbrechts, Germany) was used. All monitoring data were stored using ICM+® software (Cambridge Enterprise, Cambridge, UK, http://www.neurosurg.cam.ac.uk/icmplus). Time-averaged means for ABP, ICP CPP (ABP minus ICP), and PRx [7] were calculated and stored every minute.

Data processing and visualisation

MATLAB (The MathWorks, Inc., Natick, Massachusetts, USA) was used to implement a curve-fitting procedure based on an algorithm described elsewhere[4] in order to retrieve the PRx-CPP curves and the corresponding CPPopt values every minute, with a calculation data buffer of 4 hours . Importantly, all the fitted PRx-CPP curves were extended to cover the whole examined range of CPP, from 40 to 120 mmHg.

The sequential PRx-CPP curves were then used to create a colour-coded map of PRx-CPP relationship evolution over time (Figure 1b). The time (horizontal) axis represents the position of the moving window for CPPopt calculation. The fitted values of PRx are color-coded for every CPP-time point in the plot. The cool (blue to yellow) colors represent intact cerebral pressure reactivity while impaired pressure reactivity is represented by hot (orange to red) colors. Black areas represent time points for which no CPPopt could be determined. In the second step a non-causal, exponentially weighted moving average (EWMA) filter (n=240 data points (i.e. 240 minutes), α=0.005) was applied to the image along the time

axis only. This filter has a low-pass (smoothing) effect in time, and moreover it allows to fill in some of the gaps (of duration not exceeding the filter length) with appropriately weighted average of the preceding and following data values (Figure 1c). In a third step the measured CPP (blue line) values were smoothed with the same EWMA filter and added to the image. Finally, the boundaries of the actual CPP ranges used for individual curve fitting (reflecting the number of included CPP intervals and thereby providing a proxy of the curve reliability) are indicated with black lines. Transparent overlays on both sides of these black lines make clear within which CPP range the patient was kept and where interpolation of the PRx-CPP curves has taken place. A 'quality' indicator bar was added on top of the figure, marking sections of the image where the original gaps were present but which were subsequently interpolated by the EWMA filter (figure 2a).

Results

We illustrate the new CPPopt visualization method for the first three monitoring days of four TBI patients (Figure 2) and provide some retrospective observations that could not have been made with the traditional approach.

In patient 1 (Figure 2a), the PRx-CPP landscape indicates that lower CPP values could have probably been well tolerated on day two. By day three however PRx becomes positive over the whole CPP range (complete loss of autoregulation). In such situations, autoregulation cannot be optimised and non CPP orientated, management protocols are probably temporarily more appropriate. In patient 2 (Figure 2b) PRx became consistently negative (improving autoregulation) for CPP values around 70 mmHg on day 2 but in the later part of day 3 the patients'

autoregulation deteriorated considerably suggesting that a more aggressive and targeted management of CPP at higher values (80-90) could have perhaps been attempted. The PRx-CPP image for patient 3, (Figure 2c), tells the opposite story. The patient started off with global loss of autoregulation, then on day 2 the autoregulation seemed to have recovered but only for a relatively narrow and high (75-90) range of CPPs. Subsequently, from day 3 onwards autoregulation recovered over a broad range (55-75) of CPP. Also patient 4 (Figure 2d) started with global loss of autoregulation with the patient kept at very high CPPs (above 90) at end of day 1. Subsequently, from day 3 improved autoregulation in the range 60-75 mmHg might have enabled keeping CPP more 'stable' in this range over time.

Discussion and conclusions

In our previous work[4] we used PRx as a marker of cerebrovascular reactivity to provide a continuously updated individualised target for management of CPP, termed CPPopt. Here, we present a visualisation tool which may help clinicians understand the prevailing physiology in the context of time variation so as to help them in their decision making in individual patients.

First, by reducing the complexity of the CPP-PRx relationship to a single value (CPPopt) is an oversimplification that may omit clinically important aspects of autoregulatory behaviour. For example, in addition to a CPPopt target it is also useful to understand what the overall autoregulatory capacity is and how dependent autoregulation is on CPP. Second, the CPPopt time series may sometimes behave quite erratically with large jumps in CPPopt despite relatively stable overall clinical condition of the patient. Finally the current CPPopt

calculation does not always return a valid result at every instant leading to periods with no data (gaps).

Such observations naturally reduce the physiological relevance of any single value of CPPopt and are probably in part a consequence of the assumptions of the CPPopt calculation including the assessment of autoregulation itself using the PRx index. Since PRx (and therefore CPPopt) is calculated from spontaneous variations in ICP and ABP rather than diagnostic interventions, it is fundamentally a statistical parameter, with all uncertainties this brings.

The proposed visualisation method attempts to address and ameliorate these limitations by providing a continuous representation of the relationship between autoregulation and CPP over time. This allows for not only an indicator of the instantaneous CPPopt but also for the full appreciation of the CPP-dependence of autoregulation past and present. The erratic behaviour and 'missing values' of CPPopt is addressed by smoothly interpolating the CPP-PRx behaviour. This smoothing is physiologically plausible when we consider the timescales of the underlying pathobiology likely to be responsible for changes in autoregulation are also likely to be in the order of hours-days rather than minutes.

What we describe here is a natural extension of the concept of autoregulatory assessment, providing the full retrospective 'landscape' of PRx-CPP relationship extending over the past several hours. Although further methodological improvements and a test of functionality are needed, the proposed visualisation, while addressing some of the problems discussed above, may improve individual CPP management methods based on the status of cerebral autoregulation, current and past. The visualisation tool could be helpful in the development and

fine tuning of an autoregulation-guided CPP treatment protocol that needs prospective testing.

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Figure legends

Figure 1 Visualization of the PRx-CPP relationship and 'optimal CPP' (CPPopt) time profile: A) the original visualization showing one curve snapshot and CPPopt time trend (green line)[4]; B) consecutive PRx-CPP curves plotted using a color map, along the time axis; C) as above, but with exponential smoothing added; the final, proposed, complete visualisation image for CPPopt of this patient is in figure 2a.
ABP indicates arterial blood pressure; ICP, intracranial pressure; CPP, cerebral perfusion pressure; CPPopt, optimal cerebral perfusion pressure; PRx, pressure reactivity index; PRxopt, optimal pressure reactivity index.

Figure 2 Examples of the new visualisation method applied to 4 selected patients, over the first 3 days of monitoring: A) male, 54 years old, fall from roof, GCS of 7, GOS of 4 (moderate disability) B) male, 16 years old, RTA, GCS of 7, GOS of 5 (low disability) C) female, 19 years old, RTA, GCS of 3, GOS of 1 (Death) and D) male, 58 years old, fall of stairs, GCS of 7, GOS of 1 (Death). The blue line indicates the patients' (smoothed) CPP. The Quality Indicator (QI) above the figure shows 'grey' bars indicating interpolated PRx-CPP landscapes (with exponential smoothing) and 'black' bars representing absence of landscape data due to the set smoothing criteria. The 'transparent' areas reflect the CPP intervals where the fitted PRx-CPP curves were extended (interpolated on both sides) to cover the whole examined range of CPP from 40 to 120 mmHg. In that respect the 'black lines' represent the boundaries of the actual CPP ranges used for individual curve fitting.

GCS indicates Glasgow Coma score (after resuscitation); RTA, Road Traffic Accident; GOS, Glasgow Outcome Scale (at 6 months).

Figure 1

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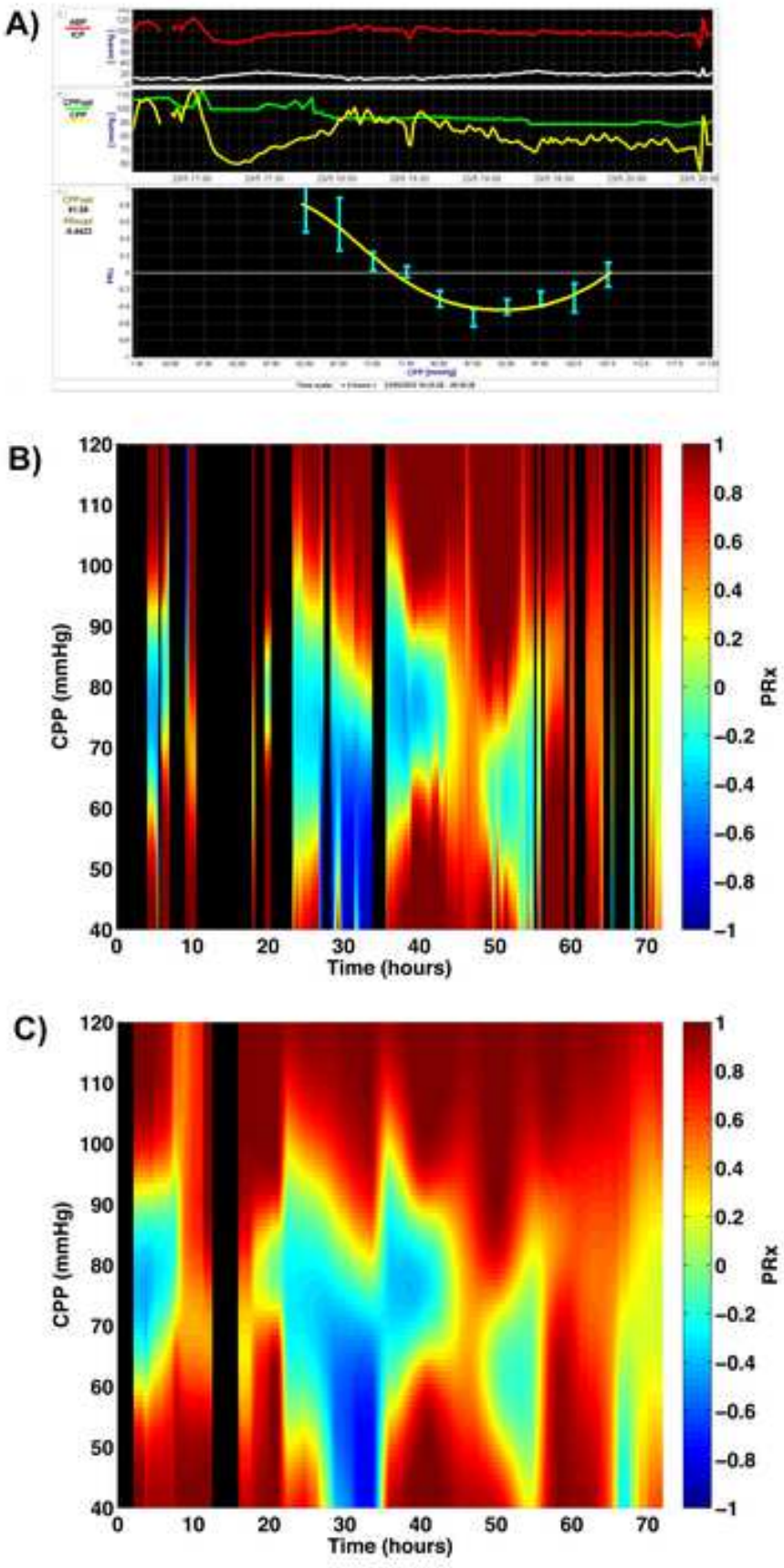

Figure 2

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