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Accuracy of non-invasive intracranial pressure measurement

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Abstract: Non-invasive measurement of intracranial pressure (ICP) reduces the complications and cost for both patient and health care systems. Improvement of non-invasive methods has led to development of systems for reproducing continuous, real-time non-invasive ICP signals. So far, non-invasive methods have been tailored for the patients with head trauma. We have used Schmidt's auto-adaptive method to assess the accuracy of this method for patients after surgery for supratentorial brain tumors. Data from forty patients with the diagnosis of brain tumor operated from 2008 to 2010 were used to estimate the accuracy of Schmidt's method in our patients. We obtained the model parameters from 30 recordings. We determined the ICP wave form for the remaining patients by both invasive and non-invasive techniques. In the test group, by invasive method, the mean ICP± 2SD was 17.1 ± 6.6 mmHg and using non-invasive method, the mean ICP ± 2SD was 16.5 ± 5.4 mmHg. The calculated error was 4.6 mmHg using root mean square errors. The average Pearson correlation between the estimated and real waveforms was 0.92. We believe that application of this method is acceptable for post-operative assessment of ICP in brain tumor patients.

Keywords: Intracranial pressure • Non-invasive • Monitoring • Brain • Tumor

1. Introduction

In contrast to most other organs, the brain is protected by a stiff bony structure. An increase in ICP may therefore impede cerebral blood flow (CBF) and cause ischemia. Raised ICP is an important secondary insult in brain-injured patients and a predictor of poor outcome after traumatic brain injury. It is used as a target in many treatment algorithms. ICP is also used to calculate CPP, which is the difference between MAP and ICP (CPP=MAP-ICP). CPP represents the pressure gradient across the cerebral vascular bed and is used as a therapeutic target for brain-injured patients in many intensive care units and is recommended by the Brain Trauma Foundation's evidence-based guideline [9,17].

Acute cerebral diseases frequently lead to elevated intracranial pressure (ICP). Monitoring of ICP could be of vital importance, ensuring the efficacy of therapeutic measures. So far, two different approaches have been used for non-invasive ICP measurements. One of them is based on the relationship between the mean ICP values and flow parameters such as Pulsatility Index (PI) and Resistance Index obtained from Trans Cranial Doppler studies (TCD). The other method is based on

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the relationship between the mean ICP and the mean invasive arterial blood pressure (ABP) adjusted by flow parameters, as described by Aaslid [1], Belford and Czosnyka [5].

The major problem with these methods is that the obtained result is the average value for each wave cycle and the ICP wave form could not be reproduced. But we know from clinical experience that the alterations in waveform could be informative for the observing caretaker to predict clinical outcome [3].

The second approach uses multiple sequential samples from invasive ABP waveform adjusted by weight functions from flow characteristic studies using TCD to reproduce ICP waveform continuously such as the Schmidt method [10]. The results of both of these methods have been validated by data from patients with traumatic brain injuries. To our knowledge, there is no publication assessing the accuracy of these methods in patients with brain tumor after surgical resection. Traumatic brain-injured (TBI) patients undergoing ICP monitoring are generally comatose, with Glasgow Coma Scale (GCS) scores blow eight, which is associated with serious brain injury and accompanying impairment of vaso-reactivity of brain vessels or osmoreceptor or auto-regulatory activity observed in normal human brains [16]. In patients with severe brain injuries, cerebral auto-regulation (CA) may become affected for a long period. Methods that relate arterial blood pressure (ABP) to cerebral blood flow velocity (FV), ignoring the contribution of ICP to cerebral perfusion pressure (CPP) are not suitable for use in patients with intracranial hypertension [6-8]. Continuous adaptation of the model to cerebral auto-regulation improves the accuracy of non-invasive estimation of ICP value and ICP dynamics [11].

On the other hand, the increase in ICP of brain tumor patients occurs gradually during several months to years. So it is accompanied by compensatory reactions from adjacent tissues. Thus one might argue against the applicability of these methods in patients after brain tumor surgery. In this study, we have addressed this issue by studying cases with brain tumors in supra-tentorial area and outside neuraxis (extra axial tumor) and measured the difference between estimated and real results. We used adaptive non-invasive estimation method proposed by Schmidt to consider the effect of altered auto-regulation observed in brain tumor patients [11-13].

We have also used only intra-ventricular catheters for invasive ICP measurement in our cases to avoid the problems with regional differences in parenchymal pressure obtained by intra-parenchymal or subarachnoid or epidural catheters [14].

2. Material and Methods

Forty patients diagnosed with supratentorial extra axial tumor operated in Shohada Tajrish Hospital were monitored and enrolled in our study. We selected patients aged 15-55 so the age-related changes in brain tissue mechanical properties could not affect the results. We also selected patients with extra-axial tumors so that the tumor infiltration into brain tissue did not affect the tissue properties. For ethical reasons, we only inserted catheters for those patients who had significant peritumoral edema or those in whom post-operative brain swelling was potentially predictable judged by the neurosurgeon. All patients were informed about the insertion of intraventricular catheter and the potential risk and benefits of such a procedure. Written informed consents were signed by each patient enrolled in our study. Also the agreement of ethical committee of our hospital had been issued before the initiation of our study. All of our patients had a GCS score of 15 before surgery.

For all patients we used intraventricular catheters manufactured by SOPHYSA Pressio® PSO-VT. The monitor we used for intraoperative zeroing was SOPHYSA PSO-3000. The data were monitored in ICU with Novin S1800 monitor manufactured by POOYANDEGAN RAH SAASAT Co. The data processing was done using a modified SAHAND Central Monitoring System specially designed by Pooyandegan Rah Saadat Company to integrate the data from ABP, ICP and TCD simultaneously. We used Esoate Mylab 2.5 MHz probe for TCD recording.

We inserted the intraventricular catheter through a Kocher burr hole at the side of the craniotomy and the catheter was zeroed prior to the insertion with a mobile Sophysa monitor in our operating room. When we encountered significant brain swelling after opening the dura matter, we aspirated 10 to 15 cc of CSF in ten minutes to obtain a suitable brain relaxation.

After tumor removal, the dura was closed occlusively in all cases and the patients were transferred to Intensive Care Unit (ICU) and the catheter was attached to the monitor setting. All patients had intraoperative intra-arterial catheter for invasive ABP recording through a transducer from radial artery at the level of the heart. If the ICP value was more than 20 mmHg, conventional methods for treating raised ICP was applied.

All recordings were performed at day 2 or 3 after surgery with the help of our ICU specialists and a neuroradiologist. We recorded simultaneous invasive ICP and ABP and FV signals for 30 minutes in each patient while the patient's head was elevated 15 to

30 degrees above his/her torso. The TCD signal was obtained by an expert neuro-radiologist . The target point was one centimeter distal to the bifurcation of middle cerebral artery (MCA) confirmed by B-mode image of our duplex device. After correct placement of ultrasound probe, it was fixed using a holder frame. The TCD signal was recorded from the contralateral MCA to avoid any disturbance in the flow of the artery caused by surgical manipulation or tumor effect.

2.1. Definition of terms and calculations

The intracranial compartment can be considered a "black box" system with an input signal, the arterial blood pressure (ABP), and an output signal, the ICP. A so-called weight function described the relationship between ABP and ICP curves. Certain parameters, called transcranial Doppler (TCD) characteristics, were calculated from the cerebral blood flow velocity (FV) and the ABP curves and were used to estimate this weight function. From simultaneously sampled FV, ABP, and (invasively measured) ICP curves of a defined group of patients with severe head injuries, the TCD characteristics and the weight function were computed. Multiple regression analysis revealed a mathematical formula for calculating the weight function from TCD characteristics. This formula was used to generate the ICP simulation.

We used adaptive non-invasive continuous estimation of ICP method proposed by Schmidt to generate ICP waveforms non-invasively from our patients [11]. This method is based on a linear system model between ICP and ABP [12]. A weight function describes relationship between ABP as input signal and ICP as output signal. To calculate these coefficients, TCD characteristics are defined. TCD characteristics consist of ABP to FV impulse response and its coefficients divided by ABP and also PI and PL. PI indicates plasticity index and PL indicates pulse length from FV signals [12].

The equation below shows the relation between parameters derived from FV and ABP waveforms.

$$W_j = B * \left(\frac{T_j}{ABP}, PI, PL \right) + B$$

TCD matrix:

$$\left(\frac{T_j}{ABP}, PI, PL \right)$$

W_j: ABP→ICP coefficients
T_j: ABP→FV coefficients
ABP: arterial blood pressure waveform
PI: pulsatility index
PL: pulse length

2.2. Non-invasive ICP simulation [11,12]

With the use of patient data, consisting of simultaneously recorded FV, ABP, and (invasively measured) ICP curves, the procedure was generated in three steps.

Step 1: Computing the weight function from the given ABP and ICP curves

The weight function between ABP and ICP curves was computed at different times of recording. To transform the ABP into the ICP curve with maximum precision during a defined time interval (in this study an interval of 14 heart cycles was chosen), a system of linear equations had to be calculated. The solution of this system of equations resulted in a vector containing the coefficients of the weight function. However, for technical reasons (regarding precision and calculation time), 25 coefficients were chosen. For a given weight function $(f_0, f_1, ..., f_{24})$, the ICP value at point k in the time sequence could be computed by the values of the ABP recorded at times k-24, k-23, ..., k-1, k according to the formula $ICP_k = f_0 * ABP_k + f_1 * ABP_{k-1} + f_{23} * ABP_{k-23} + f_{24} * ABP_{k-24}$.

Step 2: Calculation of TCD characteristics

In this study, the coefficients of a weight function between FV and ABP curves were used as TCD characteristics. The computation was similar to the one described in Step 1 and performed at the same times. For technical reasons six coefficients were used here to define the weight function instead of 25.

Step 3: Statistical processing to calculate the relationship between weight functions and TCD characteristics

The relationship between the TCD characteristics of step 2 and the 25 coefficients of the weight function in step 1 was described by an approximating linear function (i.e., a matrix **A** and a vector **B**), which was calculated through a sequence of 25 multiple regression analyses (one for each of the 25 coefficients of the weight function) of the patients' data. This process was similar to a standard linear regression between one dependent and one independent variable. In contrast to the standard situation, we had 25 dependent variables, and each of them was related to six independent variables (the TCD characteristics).

After steps 1 to 3 were performed, the non-invasive ICP simulation procedure worked as follows: While the FV and ABP curves were recorded, the TCD characteristics were computed every 10 seconds and transferred to the simulation function. Finally, the simulation function transformed the ABP curve into the simulated ICP curve.

Table 1. FV characteristics (cm/s) of the patients. (Vp= peak systolicvelocity, Vm= mean flow velocity, Ved= end diastolic flow velocity, std= standard deviation).

Vm (cm/s)	Ved (cm/s)	Vp (cm/s)	FV characteristics
161.7	124.7	225.1333	maximum
31.1	7.8	27.05	minimum
61.9	35.76869	94.311	Mean
14.65	25.69418	43.84253	Std

Table 2. Arterial Blood Pressure (ABP) characteristics of the patients. (max= maximum, min=minimum, std=standard deviation).

Peak (mmHg)	Diastole (mmHg)	Mean (mmHg)	ABP Characteristics (mmHg)
159	93	127.2860	Max
89	43	68.2795	Min
113.4571	68.2	92.0350	Mean
19.2176	16.9407	15.3649	Std

2.3. Assessment of SCA (State of Cerebral Autoregulation)

Time-averaged values of ICP, ABP, CPP (CPP_ABP_ICP), and FV were calculated from time integration for 10-second intervals. An autoregulation index (Mx) was calculated as a Pearson correlation coefficient of consecutive samples of CPP and FV mean values, i.e., every 6 minutes.

Similarly, the pressure-reactivity index (PRx) was calculated as a Pearson correlation coefficient of 36 consecutive samples of ABP and ICP. PRx is similar to Mx but takes into account active regulation in cerebral blood volume.

2.4. Non-invasive ICP assessment

The TCD characteristics are used to calculate a dynamic transformation formula connecting ICP and ABP.

The model assumes a linear relationship between TCD characteristics and the coefficients of the ABP to ICP transformation. This linear function (nICP matrix) constitutes the kernel of the nICP assessment procedure and may be constructed using the reference data consisting of FV, ABP, and direct ICP recordings from a well-defined group of patients.

2.5. Non-invasive ICP Assessment With Feedback-Controlled Adaptation to SCA

For calculation of nICP, we used a linear combination of 2 CA-specific nICP procedures. During analysis, the state of autoregulation was regularly estimated by correlation between FV and nCPP (nMx) and between ABP and nICP (nPRx). These indexes were used as feedback to fit the nICP procedure to the current SCA. A linear combination of both above-mentioned CA-specific nICP assessment procedures was computed each time from the currently estimated SCA to create the best

fitting procedure and to calculate final nICP values.

We used MATLAB 2008 for implementing adaptive non-invasive estimation of ICP [11,12]. We extracted the required parameters form 30 records of our 40 records and then we estimated non-invasive ICP for the 10 remaining records. The error was calculated using root mean squared method and Pearson correlation between the estimated ICP and the invasive recordings are also calculated.

3. Results

We used 40 recording from 22 (55%) male and 18 (48%) female patients, aged between 16 and 54 (Mean±2SD: 48.8 ±7.3 year). All patients had supratentorial meningioma. In 31 of them the meningioma was attached to the skull base and in the remaining it was attached to convexity dura or falcian area. In 27 cases (67%) the side of surgical approach was from the right and in the remaining from the left. The maximum diameter of the tumor on Magnetic Resonance Imaging (MRI) with contrast was ranged from 32 mm to 74 mm (Mean ± 2SD: 52.5 ± 4.8mm). All patients selected had at least 20 mm peritumoral edema in which we had predicted the possibility of post-operative brain swelling. On the day of recording invasive systolic ABP ranged between 89 mmHg and 159 mmHg (Mean ±2 SD: 113.4± 38.4) and diastolic ABP ranged between 43 mmHg and 93 mmHg (Mean±2SD: 68.2 ±33.8 mmHg) and mean ABP ranged between 68.2 and 127.2 (Mean±2SD: 92.0± 30.6mmHg). The mean of flow velocity ranged from 31.1 cm/s to 161.7 cm/s (Mean±2SD: 61.9 ± 29.3 cm/s).

In every machine learning and modeling method we need most of our data to train the system and calculate system parameters (30 cases in our study).

Table 3. ICP characteristics (mm Hg) in all of the patients (40 cases). (max= maximum, min=minimum).

ICP Parameters(mm Hg)	Range(mm Hg)	Average(mm Hg)
Max ICP	20-25	22.8460
Min ICP	10-15	12.8460
Mean ICP	15.0571- 20.4857	18.1470

Table 4. ICP characteristics (mm Hg) in the 30 patients by the invasive technique to train the software. (max= maximum, min=minimum).

ICP Parameters (mm Hg)	Range (mm Hg)	Average (mm Hg)
Max ICP	20-24	22.8340
Min ICP	11-15	12.8530
Mean ICP	16.0432- 20.4857	18.1670

Table 5. ICP characteristics (mm Hg) in the test group (10 patients), measured by invasive technique. (max= maximum, min=minimum).

ICP (mm Hg)	Range(mm Hg)	Average(mm Hg)
Max ICP	21-25	23.8520
Min ICP	10-14	12.7394
Mean ICP	15.0571- 20.4322	17.1323

Table 6. ICP characteristics (mm Hg) in the test group (10 patients), measured by non-invasive technique. (max= maximum, min=minimum).

ICP (mm Hg)	Range(mm Hg)	Average(mm Hg)
Max ICP	21.3-24.6	21.7590
Min ICP	10.9-13.8	12.6556
Mean ICP	14.9- 20.3	16.5341

To understand how good our method works, we used the rest of our data (10 cases) to examine the system and to find out differences between actual values and estimated values calculated by machine (software). Selection of 30 records among 40 records was completely random. The average invasive ICP for all patients (40 cases) ranged from 12.8 to 22.8 mmHg (Mean ± 2SD: 18.1 ± 6.4 mmHg). We obtained the model parameters from 30 recordings and estimated the ICP wave form for the remaining 10 patients. In the first group (30 cases), the average invasive ICP values ranged from 12.9-22.7 mmHg (Mean ± 2SD: 18.2 ± 6.2 mmHg).
In the second group (10 cases), ICP parameters were determined by both invasive and non-invasive techniques.

The average ICP values in this group measured by invasive method, ranged from 12.7-23.8 mm Hg (Mean ± 2SD: 17.1 ± 6.6 mmHg).

Using non-invasive method, the obtained average ICP values in the second group (10 cases)r anged from 12.6-21.7 mm Hg (Mean ± 2SD: 16.5 ± 5.4 mmHg).

The calculated error was 4.6 mmHg using root mean square error. The average Pearson correlation between the estimated and real waveforms was 0.92. All statistics of our recordings summarized in Tables 1-6.

4. Discussion

Non-invasive estimation of intracranial pressure with considering cerebral auto-regulation and vasoreactivity as formulated in adaptive Schmidt method has enabled us to estimate the intracranial pressure in patients with serious traumatic brain injury in whom the physiological mechanisms involved in ICP has been critically impaired [14]. Also the flexibility of this method ensures correction for different states of cerebral auto-regulation during the recording.

Previously described methods were based upon data of patients with traumatic brain injuries, but the applicability of the results for other groups of patients have not been analyzed [1,5,17].

As Schmidt himself had proposed, the application of his method to other groups of patients needed further investigations. He tested his model on 10 patients with hemorrhagic stroke and found the results encouraging [11].

According to the Schmidt's study, the head injured patients who underwent ICP monitoring were comatose [14]. These cases had severe brain injury and impaired vasoreactivity of brain vessels. It should be noticed that in patients with brain tumor the increase in intracranial pressure occurs gradually from month to years which in turn is accompanied by compensatory reactions from adjacent tissues. Thus, the applicability of the methods used in post-traumatic patients to post-operative cases is in question [2].

According to the literature, the effect of elective tumor resection on cerebral autoregulation and CO2 reactivity may be different [4]. According to the previous literature, pre-operative cerebral auto-regulation was impaired in a significant number of patients with large supratentorial tumor size and midline shift more than 5 mm and was associated with post-operative impaired cerebral auto-regulation during the first 24 hours after the surgery [15]. In this study we tested the applicability of the method on patients with brain tumor after surgical resection. We had our recordings on day 2 or 3 after the surgery in a period with the maximum risk for post-operative events that leads to increased ICP. These events include post-operative brain swelling, delayed bleeding or venues thrombosis. The model revealed itself to be able to reproduce ICP and cerebral hemodynamics in this group of patients. We believe that this returns to the important

fact that the software can sense the cerebral vascular response to changes in systemic arterial pressure. Our patients had other specific characteristics. They were all conscious and on their own respiration on the day of recording, so the average CO2 pressure in their blood was a bit higher hat those of trauma patients. In our patients it was about 35 to 40 mmHg while in Schmidt's patients it was about 30 to 40 mmHg [14]. This might be due to the fact that hyperventilation is used to decrease ICP in trauma patients. Also trauma patients which are monitored for intracranial pressure have a GCS <8 and mechanically ventilated. This is associated with the use of sedative agents and muscle relaxant which are routinely administered to these patients to keep them under ventilator [14]. We know that these agents have

drastic effects on hemodynamic features of the brain and can shift the pressure volume curve of the brain from its normal position. But with all these differences the model came out valid in predicting the ICP in a different group of patients.

5. Conclusions

According to this study autoregulation is considered a significant factor in accuratre estimation of intracranial pressure. Non-invasive monitoring of intracranial pressure using adaptive Schmidt model can be used accurately in patients with brain tumor after surgical resection.

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