2021 43rd Annual International Conference of the
IEEE Engineering in Medicine & Biology Society (EMBC)
Oct 31 - Nov 4, 2021. Virtual Conference

Analysis of the Shape of Intracranial Pressure Pulse Waveform in Traumatic Brain Injury Patients

Agnieszka Kazimierska[1], Agnieszka Uryga [1], Cyprian Mataczyński[2], Małgorzata Burzyńska[3], Arkadiusz Ziółkowski[1], Andrzej Rusiecki[2], and Magdalena Kasprowicz[1]

Abstract— **Intracranial pressure (ICP) pulse waveform, i.e., the shape of the ICP signal over a single cardiac cycle, is regarded as a potential source of information about intracranial compliance. In this study we aimed to compare the results of automatic classification of ICP pulse shapes on a scale from normal to pathological with other ICP pulse–derived metrics. Additionally, identification of artifacts was performed simultaneously with pulse classification to assess the effect of artifact removal on the results. Data from 35 traumatic brain injury (TBI) patients were analyzed retrospectively in terms of dominant waveform shape, mean ICP, mean amplitude of ICP (AmpICP), mean index of compensatory reserve (RAP index), and their association with the patient's clinical outcome. Our results show that patients with poor outcome exhibit more pathological waveform shape than patients with good outcome. More pathological ICP pulse shape is associated with higher mean ICP, mean AmpICP, and RAP.**

Clinical relevance— **In the clinical setting, ICP pulse waveform analysis could potentially be used to complement the commonly monitored mean ICP and improve the assessment of intracranial compliance in TBI patients. Artifact removal from the ICP signal could reduce the frequency of false positive detection of clinically adverse events.**

I. INTRODUCTION

Traumatic brain injury (TBI) is considered an important public health concern because of its high incidence and significant socioeconomic costs [1]. In the clinical setting, monitoring of mean intracranial pressure (ICP) is often used in the management of TBI patients due to the association between increases in ICP and higher mortality and worse outcome [2]. However, pressure (P) and volume (V) in the intracranial space are nonlinearly related (mathematically modelled as an exponential P-V curve), and a reduction in brain compliance (i.e., the cerebrospinal system's ability to compensate changes in volume without potentially threatening increases in ICP) may occur before a rise in mean ICP is detected [3].

Various studies have been conducted to develop tools for the assessment of intracranial compliance. A number of such studies included the analysis of ICP pulse waveform, i.e., the ICP signal over a single cardiac cycle. Notably, there have been attempts to derive that information from changes in the amplitude of the ICP pulse (AmpICP) and its relationship with changes in the mean value [4], [5] or from changes in the configuration of peaks and notches of ICP pulse contour [6], [7]. The RAP index [5], which is the correlation coefficient between changes in mean ICP and AmpICP, is a clinically accepted method of assessing cerebral compensatory reserve that provides an estimation of the patient's position along the P-V curve. However, peak detection methods proposed so far are yet to gain widespread clinical application. More recently, a different approach was suggested, which is based on classification of different shapes of the ICP pulse waveform using a neural network [8] instead of relying on the results of peak identification. In this work we aimed to compare the results of pulse waveform classification using a previously developed deep learning model with other metrics used to describe TBI patients and to assess the possible relationship between ICP pulse type and the patients' outcome.

II. MATERIALS AND METHODS

A. Data collection

This study was performed as a retrospective single-center trial at Wroclaw University Hospital (Wroclaw, Poland) with approval from the local Ethics Committee (approval no. KB-624/2014) and in adherence to the Declaration of Helsinki. 35 patients suffering from TBI were selected for analysis. All patients were treated according to guidelines applicable at the time of admission [9]. The study group was homogenous with regard to severity of the injury and treatment protocol. The patients' condition was assessed using the Glasgow Coma Scale (GCS), Marshall scale, and Rotterdam scale. The patients' outcome was assessed using the Glasgow Outcome Scale (GOS) at 3 months after discharge from the hospital, with poor outcome represented by scores I–III and good outcome by scores IV–V.

ICP was measured invasively using an intraparenchymal sensor (Codman MicroSensor ICP Transducer, Codman & Shurtleff, MA, USA) inserted into the frontal cortex. The

*Research supported by the National Science Centre, Poland (grant no. UMO-2019/35/B/ST7/00500). A. Uryga is supported by the Foundation for Polish Science. The funders had no role in study design or preparation of this submission.

[1]A. Kazimierska (corresponding author; phone: +48 71 320 46 65; agnieszka.kazimierska@pwr.edu.pl), A. Uryga, A. Ziółkowski, and M. Kasprowicz are with the Department of Biomedical Engineering, Wroclaw University of Science and Technology, 27 Wybrzeże Wyspiańskiego street, 50-370 Wroclaw, Poland. agnieszka.uryga@pwr.edu.pl, arkadiusz.ziolkowski@pwr.edu.pl, magdalena.kasprowicz@pwr.edu.pl

[2]C. Mataczyński and A. Rusiecki are with the Department of Computer Engineering, Wroclaw University of Science and Technology, 27 Wybrzeże Wyspiańskiego street, 50-370 Wroclaw, Poland. cyprian.mataczyński@pwr.edu.pl, andrzej.rusiecki@pwr.edu.pl

[3]M. Burzyńska is with the Department of Anaesthesiology and Intensive Care, Wroclaw Medical University, 213 Borowska street, 50-556 Wroclaw, Poland. malgorzata.burzynska@umed.wroc.pl

signal was recorded with sampling frequency of 200 Hz using ICM+ software (Cambridge Enterprise Ltd, Cambridge, UK). The patients were monitored continuously, starting in day 1 or day 2 after admission to the hospital, depending on the date of surgery. On average, the patients were monitored for 5 ± 3 days.

B. Signal analysis and ICP pulse waveform classification

All analyses were performed using programs custom written in Python 3.8 with PyTorch package. A residual neural network (ResNet) model using 1-D vector of signal samples (standardized to an interval between 0 and 1 and resampled to uniform length of 180 samples) was trained to classify ICP pulse waveforms into four morphological classes: 1– normal, 2 – possibly pathological, 3 – likely pathological, 4 – pathological, reflecting the changes in the configuration and visibility of characteristic peaks P1, P2, and P3 of the waveform (Fig. 1) [8]. An additional class (A+E) was introduced to identify invalid pulses in the signal, such as artifacts or errors in pulse onset detection. Pulse detection was performed using modified Scholkmann algorithm [10]. The model was trained using 23252 waveforms (divided into training and validation datasets of 17011 and 6241 pulses, respectively) randomly selected from full recordings of TBI patients and manually classified by an expert researcher. All waveforms from the same patient were assigned to only one of the datasets to prevent correlation between datasets that could limit the model's generalization ability.

The model was then tested in an independent dataset of 650 pulses extracted from 11 aneurysmal subarachnoid hemorrhage patients and manually classified by a panel of three experts (who showed significant agreement as tested by Fleiss kappa test, κ=0.700 (95% CI: 0.672 to 0.728), $p < 0.001$) to ensure its applicability to patient cohorts with different data distributions. In cases with waveform type at the border between two classes two labels were allowed, and during assessment of classification accuracy the label produced by the model was considered correct if it matched either of the two. A detailed description of model development and evaluation methodology is presented in our earlier paper [11].

Classification results were obtained for all pulses in the full recordings of TBI patients using the ResNet model with each patient characterized by dominant pulse type (i.e., the pulse type occurring most frequently in the whole recording with pulses classified as artifacts excluded from analysis). The long-term recordings were also used to obtain RAP index [5] with AmpICP calculated as the amplitude of the fundamental component of the ICP signal in range 0.6–1.8 Hz using Fast Fourier Transform. The interpretation of the RAP index is as follows: values around 0 indicate good compensatory reserve whereas values increasing to +1 indicate poor compensatory reserve; negative values are associated with cessation of blood flow due to the collapse of cerebral arterial bed at very high ICP [12]. Mean ICP and mean AmpICP were calculated in 10-second-long windows and the correlation coefficient between them was calculated in 5-minute-long windows shifted every 10 seconds. The calculations were performed for each raw recording and for modified recordings where the pulses identified by the model as artifacts were removed. Finally, episodes of mean ICP exceeding 20 mm Hg and episodes of RAP exceeding 0.6 (with minimum length of each episode no less than 5 minutes) were identified in each recording before and after artifact removal. The thresholds reflect values used in clinical practice to identify intracranial hypertension [9] and reduced compensatory reserve [13], respectively. Total duration of all identified episodes was analyzed as well as the number of individual episodes and mean duration of a single episode.

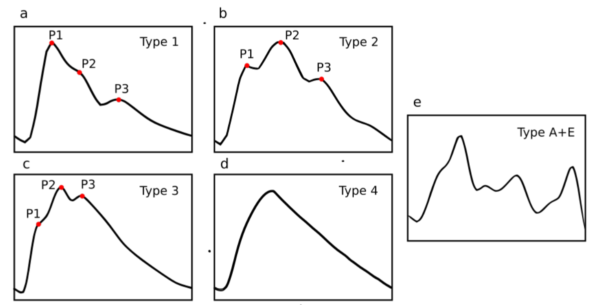

Fig. 1. Illustrative examples of ICP pulse waveform shapes in each class: a) 1 – normal, b) 2 – possibly pathological, c) 3 – likely pathological, d) 4 – pathological, e) A+E – artifact or error.

C. Statistical analysis

Statistical analysis was performed using Statistica software (v13.1, Tibco, Palo Alto, CA, USA). Statistical significance level of 0.05 was assumed in all analyses. Data distributions were tested for normality using the Kolmogorov-Smirnov test with Lillefors correction. Difference between two independent outcome groups was assessed using Mann-Whitney U test and difference between metrics derived from recordings before and after artifact removal (i.e., dependent variables) using Wilcoxon singed rank test. The Fisher-Freeman-Halton exact test of independence was used to determine the association between two categorical variables (outcome vs. dominant pulse waveform type) with 2x4 contingency table, where the effect size was assessed using V Cramer's coefficient. The relationships between pulse type and mean ICP, mean AmpICP, and mean RAP averaged over the whole recording were calculated using multiple linear or linearized regression analysis with subjects treated as categorical factors using dummy variables (with respect to the inter-subject variability) and using partial coefficient (Rp) between analyzed variables. All results are presented as median ± interquartile range unless otherwise indicated.

III. RESULTS

A. Patient characteristics

The study group consisted of 26 men and 9 women with median age of 38 ± 29 years. All patients had comparable GCS score with median 6 ± 4. Detailed patient characteristics are presented in Table I.

TABLE I

PATIENT CHARACTERISTICS

Clinical feature	**Number of patients / Value** total group n = 35 (100%)
GCS on admission n (%)	**3-8:** 30 (86%), **9-12:** 3 (8%), **13-15:** 2 (6%)
Marshall score median ± IQR	3 ± 3
Rotterdam score median ± IQR	4 ± 1
30-days mortality n (%)	4 (10%)
GOS (3 months) n (%)	**I-III:** 20 (57%), **IV-V:** 15 (43%)

B. Classification results

The ResNet model achieved classification accuracy of 95% in the validation dataset and 81% in the independent test dataset. Detailed scores for each pulse type are presented in Table II.

TABLE II

RESNET MODEL PERFORMANCE

	Validation dataset n = 6241		**Test dataset** n = 650	
Pulse type	**Precision**	**Recall**	**Precision**	**Recall**
1	0.97	0.96	0.86	0.93
2	0.90	0.94	0.71	0.92
3	0.89	0.87	0.71	0.95
4	0.85	0.91	0.84	0.57
A+E	0.99	0.92	0.98	0.46

C. Relationship between outcome, ICP pulse type, and other metrics

There were no statistically significant differences in mean ICP, mean AmpICP, or mean RAP between good and poor outcome groups (see Table III). Dominant ICP pulse type was significantly lower (Z = 2.93, p = 0.003) in the good outcome group (1.0 ± 1.0) compared to the poor outcome group (2.0 ± 2.0). Additionally, there was a significant association between ICP pulse type and the following parameters: mean ICP (Rp = 0.63, $p < 0.001$), mean AmpICP (Rp = 0.61, $p < 0.001$), and mean RAP (Rp = 0.26, p = 0.004), as presented in Fig. 2.

Dominant ICP pulse type (see Fig. 3) was significantly associated with outcome: $\chi^2(3) = 10.11$, p = 0.011, with V Cramer's coefficient of 0.56 indicating a strong effect of this relationship. Patients in the good outcome group frequently exhibited dominant ICP pulse type 1 (73.3% of patients) and rarely types 3 or 4 (7.3% and 0.0%, respectively). On the other hand, a significant number of patients with poor outcome exhibited pulse types 3 (15.0%) and 4 (30.0%).

TABLE III

MEAN ICP, AMPICP, RAP INDEX AND DOMINANT ICP PULSE TYPE FOR PATIENTS WITH POOR AND GOOD OUTCOME. NS - RESULT NOT STATISTICALLY SIGNIFICANT

GOS after 3 months	**Poor outcome** n = 20	**Good outcome** n = 15	***p***
ICP [mm Hg]	13.88 ± 5.69	12.31 ± 4.52	ns
AmpICP [mm Hg]	1.15 ± 0.74	0.87 ± 0.54	ns
RAP [a.u.]	0.32 ± 0.23	0.46 ± 0.27	ns
Dominant pulse type	2.0 ± 2.0	1.0 ± 1.0	0.003

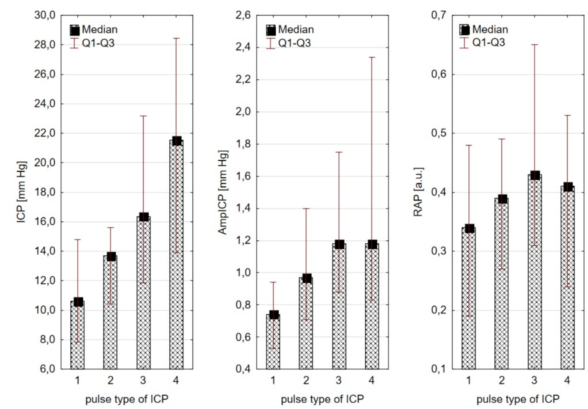

Fig. 2. The relationship between dominant ICP pulse type and mean ICP (left), mean AmpICP (middle), and RAP index (right).

D. Effect of artifact removal

For episodes of RAP > 0.6, artifact removal resulted in a statistically significant decrease in the total duration of the episodes (from 29.7 ± 37.6 hours to 25.3 ± 38.2 hours, $p << 0.001$) and in the number of individual episodes (from 141 ± 135 to 125 ± 156, $p < 0.001$). For episodes of intracranial hypertension (ICP > 20 mm Hg), artifact removal resulted in a decrease in the total duration of the episodes (from 174 ± 804 minutes to 160 ± 750 minutes, p = 0.006).

IV. DISCUSSION

In this work we aimed to use a deep learning model to classify different shapes of ICP pulse waveforms and compare them with other ICP pulse–derived indices in order to further explore the meaning of ICP pulse morphology.

Our results show that in TBI patients dominant ICP pulse type is associated with the patients' outcome. Patients in the good outcome group more frequently exhibit normal waveforms (type 1) with dominant peak P1. In the poor outcome group the number of normal waveforms decreases in favor of pathologically changed pulses, particularly rounded pulses with no identifiable peaks (type 4). In the clinical setting, ICP–guided management mostly relies on a set threshold for mean ICP above which therapeutic interventions should be introduced [15]. The application of a general

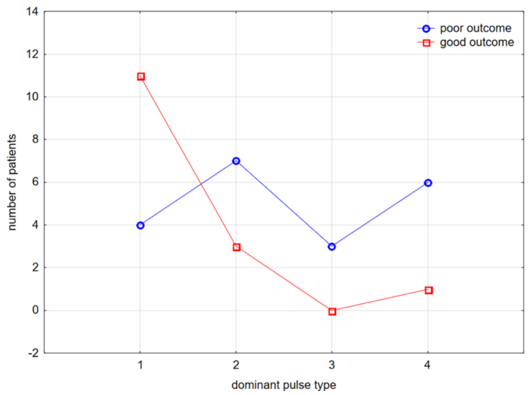

Fig. 3. The interaction between dominant ICP pulse type and the number of patients with poor or good outcome.

threshold in all TBI patients remains controversial [16], and attention has been called to the fact that the relationship between the state of the craniospinal system and mean ICP is not straightforward [3]. Accordingly, our results show that despite comparable mean ICP, the poor and good outcome groups show differences in dominant pulse type, and pulse type is the only parameter whose changes reach statistical significance when compared against outcome. Furthermore, ICP pulse types are significantly correlated with both ICP and AmpICP, reflecting the trends expressed by the pressure–volume and amplitude–pressure curves. Statistically significant but weak correlation between ICP pulse shape and RAP index may be explained by their different interpretation, as ICP pulse shape is more related to intracranial compliance while RAP provides information on the patient's position on the P-V curve. We also found that identification of artifacts simultaneously with the classification of valid pulses changes the total duration of detected episodes of increased ICP and RAP, which is in line with previous studies highlighting the role of artifacts in generating false alarms in the clinical setting [17].

Presented observations are based on the results of a preliminary study conducted in a small patient cohort and with a simple neural network model. Performance of the model can potentially be further improved by providing a more balanced training and validation dataset or by introducing modifications to the classification criteria which in their current form were derived from patients with a different type of intracranial pathology.

V. CONCLUSION

Analysis of brain compliance by means of automatic ICP pulse shape classification is a promising approach to continuous monitoring of the state of the compensatory reserve that could be used in patients with intracranial pathologies alongside standard mean ICP measurement and improve the assessment of the state of the intracranial space. Results of this study suggest an association between dominant ICP waveform type and the clinical outcome of TBI patients. Clinical significance of proposed approach should be confirmed in a larger set of patients.

REFERENCES

[1] M. C. Dewan, A. Rattani, S. Gupta, R. E. Baticulon, Y. Hung, M. Punchak, A. Agrawal, A. O. Adeleye, M. G. Shrime, A. M. Rubiano, J. V. Rosenfeld, and K. B. Park, "Estimating the global incidence of traumatic brain injury," J. Neurosurg., vol. 130, no. 4, pp. 1080–1097, Apr. 2019, doi: 10.3171/2017.10.JNS17352.

[2] S. Badri, J. Chen, J. Barber, N. R. Temkin, S. S. Dikmen, R. M. Chesnut, S. Deem, N. D. Yanez, and M. M. Treggiari, "Mortality and long-term functional outcome associated with intracranial pressure after traumatic brain injury," Intensive Care Med., vol. 38, no. 11, pp. 1800–1809, Nov. 2012, doi: 10.1007/s00134-012-2655-4.

[3] T. Heldt, T. Zoerle, D. Teichmann, and N. Stocchetti, "Intracranial pressure and intracranial elastance monitoring in neurocritical care," Annu. Rev. Biomed. Eng., vol. 21, pp. 523–551, June 2019, doi: 10.1146/annurev-bioeng-060418-052257.

[4] J. Szewczykowski, S. Sliwka, A. Kunicki, P. Dytko, and J. Korsak-Sliwka, "A fast method of estimating the elastance of the intracranial system," J. Neurosurg., vol. 47, no. 1, pp. 19–26, July 1977, doi: 10.3171/jns.1977.47.1.0019.

[5] M. Czosnyka, E. Guazzo, M. Whitehouse, P. Smielewski, Z. Czosnyka, P. Kirkpatrick, S. Piechnik, and J. D. Pickard, "Significance of intracranial pressure waveform analysis after head injury," Acta Neurochir. (Wien)., vol. 138, no. 5, pp. 531–542, 1996, doi: 10.1007/BF01411173.

[6] E. R. Cardoso, J. O. Rowan, and S. Galbraith, "Analysis of the cerebrospinal fluid pulse wave in intracranial pressure," J. Neurosurg., vol. 59, no. 5, pp. 817–821, Nov. 1983, doi: 10.3171/jns.1983.59.5.0817.

[7] C. S. Robertson, R. K. Narayan, C. F. Contant, R. G. Grossman, Z. L. Gokaslan, R. Pahwa, P. Caram Jr, R. S. Bray, and A. M. Sherwood, "Clinical experience with a continuous monitor of intracranial compliance," J. Neurosurg., vol. 71, no. 5 Pt 1, pp. 673–680, Nov. 1989, doi: 10.3171/jns.1989.71.5.0673.

[8] C. G. Nucci, P. De Bonis, A. Mangiola, P. Santini, M. Sciandrone, A. Risi, and C. Anile, "Intracranial pressure wave morphological classification: automated analysis and clinical validation," Acta Neurochir. (Wien)., vol. 158, no. 3, pp. 581–588, Mar. 2016, doi: 10.1007/s00701-015-2672-5.

[9] Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons, "Guidelines for the management of severe traumatic brain injury," J. Neurotrauma, vol. 24 Suppl 1, pp. S1-106, doi: 10.1089/neu.2007.9999.

[10] S. M. Bishop and A. Ercole, "Multi-scale peak and trough detection optimised for periodic and quasi-periodic neuroscience data," Acta Nerochirurgica Suppl., vol. 126, pp. 189–195, 2018, doi: 10.1007/978-3-319-65798-1_39.

[11] C. Mataczynski, A. Kazimierska, A. Uryga, M. Burzynska, A. Rusiecki, and M. Kasprowicz, "End-to-end automatic morphological classification of intracranial pressure pulse waveforms using deep learning," IEEE J. Biomed. Health Inform., June 2021, published online ahead of print, doi: 10.1109/JBHI.2021.3088629.

[12] L. Calviello, J. Donelly, D. Cardim, C. Robba, F. A. Zeiler, P. Smielewski, and M. Czosnyka, "Compensatory-reserve-weighted intracranial pressure and its association with outcome after traumatic brain injury," Neurocrit. Care, vol. 28, no. 2, pp. 212–220, Apr. 2018, doi: 10.1007/s12028-017-0475-7.

[13] L. A. Steiner, M. Balestreri, A. J. Johnston, J. P. Coles, P. Smielewski, J. D. Pickard, D. K. Menon, M. Czosnyka, "Predicting the response of intracranial pressure to moderate hyperventilation'," Acta Neurochir. (Wien)., vol. 147, no. 5, pp. 477–483, May 2005, doi: 10.1007/s00701-005-0510-x.

[14] M. Czosnyka and G. Citerio, "Brain compliance: the old story with a new 'et cetera,'" Intensive Care Med., vol. 38, no. 6, pp. 925–927, June 2012, doi: 10.1007/s00134-012-2572-6.

[15] C. Hawthorne and I. Piper, "Monitoring of intracranial pressure in patients with traumatic brain injury," Front. Neurol., vol. 5, pp. 121, July 2014, doi: 10.3389/fneur.2014.00121.

[16] M. Czosnyka, P. Smielewski, I. Timofeev, A. Lavinio, E. Guazzo, P. Hutchinson, and J. D. Pickard, "Intracranial pressure: more than a number," Neurosurg. Focus, vol. 22, no. 5, p. E10, May 2007, doi: 10.3171/foc.2007.22.5.11.

[17] M. Imhoff and S. Kuhls, "Alarm algorithms in critical monitoring," Anesth. Analg., vol. 102, no. 5, pp. 1525–1537, May 2006, doi: 10.1213/01.ane.0000204385.01983.61.