Intraspinal pressure and spinal cord perfusion pressure after spinal cord injury: an observational study

Georgios V. Varsos, MSc,1 Melissa C. Werndle, MRCS,2 Zofia H. Czosnyka, PhD,1 Peter Smielewski, PhD,1 Angelos G. Kolias, MRCS,1 Isaac Phang, MRCS,2 Samira Saadoun, PhD,2 B. Anthony Bell, MD, FRCS,2 Argyro Zoumprouli, MD,3 Marios C. Papadopoulos, MD, FRCS(SN),2 and Marek Czosnyka, PhD1,4

1Division of Neurosurgery, Department of Clinical Neurosciences, Addenbrooke’s Hospital, University of Cambridge, Cambridge; 2Academic Neurosurgery Unit, St. George’s University of London; 3Department of Anaesthesia, St. George’s Hospital, London, United Kingdom; and 4Institute of Electronic Systems, Warsaw University of Technology, Warsaw, Poland

OBJECT In contrast to intracranial pressure (ICP) in traumatic brain injury (TBI), intraspinal pressure (ISP) after traumatic spinal cord injury (TSCI) has not received the same attention in terms of waveform analysis. Based on a recently introduced technique for continuous monitoring of ISP, here the morphological characteristics of ISP are observationally described. It was hypothesized that the waveform analysis method used to assess ICP could be similarly applied to ISP.

METHODS Data included continuous recordings of ISP and arterial blood pressure (ABP) in 18 patients with severe TSCI.

RESULTS The morphology of the ISP pulse waveform resembled the ICP waveform shape and was composed of 3 peaks representing percussion, tidal, and dicrotic waves. Spectral analysis demonstrated the presence of slow, respiratory, and pulse waves at different frequencies. The pulse amplitude of ISP was proportional to the mean ISP, suggesting a similar exponential pressure-volume relationship as in the intracerebral space. The interaction between the slow waves of ISP and ABP is capable of characterizing the spinal autoregulatory capacity.

CONCLUSIONS This preliminary observational study confirms morphological and spectral similarities between ISP in TSCI and ICP. Therefore, the known methods used for ICP waveform analysis could be transferred to ISP analysis and, upon verification, potentially used for monitoring TSCI patients.

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ABBREVIATIONS ABP = arterial blood pressure; CPP = cerebral perfusion pressure; ICP = intracranial pressure; ISCoPE = Injured Spinal Cord Pressure Evaluation; ISP = intraspinal pressure; PRx = pressure reactivity index; SCPP = spinal cord perfusion pressure; sPRx = spinal PRx; TBI = traumatic brain injury; TSCI = traumatic spinal cord injury.


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situations can provide valuable information concerning the condition of the spinal cord in cases of TSCI.

While waveform analysis of ICP has been conducted for years and has been proven to be helpful in the management of TBI patients, very little is known about ISP in the acute phase following TSCI where its management focuses on spine realignment and fixation without taking into account ISP. The underlying reason behind this is the absence of a safe and reliable long-term monitoring technique for measuring ISP, because techniques such as Queckenstedt’s maneuver, which was being used to examine spinal fluid dynamics in TSCI, were replaced by imaging modalities (e.g., MRI or CT scanning) which in turn are not suitable for long-term monitoring. This issue was addressed recently with the introduction of a novel technique for continuously monitoring ISP at the injury site, which has allowed discussions on using ISP for managing TSCI in a similar way that ICP is used to manage TBI. Based on the abovementioned similarities between the injured brain and spinal cord, it is vital to recapitulate how the information included in the time-dependent components of ICP is crucial for understanding intracranial pathophysiology. This may form the basis for similar analyses on monitoring ISP.

ICP is derived from 3 main components: the circulation of the CSF and cerebral blood, and volumetric changes in brain tissue. According to Davson’s equation, the component associated with CSF circulation is also related to cerebral venous outflow. Expressing the cerebral blood component quantitatively has been far more difficult. It has been defined as the “vascular component” of the ICP waveform and is known to be related to cerebral blood volume and arterial blood pulsatile flow. Any factor that disturbs the CSF or cerebral blood circulation, like brain swelling or space-occupying mass lesions, may result in increases in ICP.

The waveform of ICP consists of slow fluctuations and regular respiratory and pulse waves that are seen at different frequencies (low to high frequency, respectively). Its pulse waveform contains 3 peaks—percussion, tidal, and dicrotic—with the relationship between the tidal and percussion peaks describing brain compliance. Secondary indices of ICP can be descriptive of the cerebrospinal compensatory reserve (RAP index), or—based on the interactions between the slow waves of ICP and ABP—can characterize the status of the cerebrovascular pressure reactivity (PRx index). In TBI cases, both ICP and its derived indices are well known to have a strong association with outcome and are part of the clinical assessment for deciding the therapeutic management of a patient.

Based on the inherent similarities with ICP, this observational study aims to qualitatively describe the biophysics of ISP and explore its morphology regarding different components in the time and frequency domains.

Methods

This retrospective study included prospectively collected data from 18 patients (age range 18–70 years) with severe TSCI (American Spinal Injury Association Grades A–C) who were referred to the Neurosurgery Units of St. George’s and King’s College hospitals in London and recruited to participate in the ISCoPE (Injured Spinal Cord Pressure Evaluation) study. Approval was obtained from the local research ethics committee at St. George’s Hospital in London. The details of the ISCoPE study have been described before and are briefly recapitulated here.

For ISP measurement, a Codman probe was placed subdurally following laminectomy or small laminotomy. Monitoring of ISP started within 72 hours of TSCI and continued for up to a week. In regards to the placement of the probe, after reducing and fixing the spinal fracture and inserting metalwork to stabilize the spine, a 14-gauge introducer was used to tunnel the Codman probe through the skin into the wound. A 21-gauge needle, which was bent at 90°, was used to perforate the dura at 1 level below the injury. To monitor ISP, the Codman probe was calibrated and advanced through the dural hole until the probe tip was at the site of maximal spinal cord swelling according to the MRI scan, and satisfactory probe position was confirmed with CT before data collection. In 4 patients, additional probes were inserted for simultaneous monitoring of both subdural and extradural pressure.

Regarding the effect of therapeutic interventions on ISP, changes in arterial PCO2, sevoflurane dose, and mannitol administration were not found to have any significant effects on ISP or SCPP. Increasing the inotrope dose significantly increased SCPP. Bony realignment and laminectomy did not effectively lower ISP, with laminectomy being potentially detrimental by exposing the swollen spinal cord to compression forces applied to the skin.

Imaging assessment of ISP was not studied in this cohort because, as in TSCI, spinal cord imaging may be uninterpretable because of spinal instrumentation, thus making it difficult to use imaging examinations to guide TSCI management.

ABP was measured using a radial artery catheter that was calibrated at the same horizontal level as the injured segment of the spinal cord. Probes were connected to a Codman ICP box linked via a ML 221 amplifier to PowerLab running LabChart (v. 7.3.3, AD Instruments). Further details regarding the clinical methods and surgical technique were recently published. ISP and ABP data were simultaneously captured at 100 Hz and then imported to ICM+ software (Cambridge Enterprise; http://www.neurosurg.cam.ac.uk/icmplus/) for further analysis.

Visual inspection, time averaging, and spectral analysis were performed to assess similarities in the ISP waveforms to known ICP recordings determined by our previous studies.

Analysis of the ISP Waveform

The ISP waveform can be analyzed by focusing on the signal’s time evolution in the respective monitoring period. Monitoring can last from seconds to hours or days; however, like ICP, ISP can be very unstable, and, therefore, longer monitoring periods are essential in order to gain a clear idea of the ISP trends. In that case, averaging the ISP signal over a short period of time (e.g., a 10-second time window) can provide a smooth trend for the mean ISP that has been filtered for noisy signals. The same logic
applies to ABP, and a relevant time window is needed to determine the average value of the signal. SCPP is calculated as ABP minus ISP. Important fluctuations, like slow waves and respiratory and pulse waves, can be visualized using spectral analysis of the frequency domain and short-term fast Fourier transform. The amplitude of ISP (I1) is derived from the fundamental component (first harmonic) of the pulse wave in the ISP signal.

**sPRx and sRAP Indices for ISP**

In TBI, analysis of the ISP waveform using the PRx and RAP indices can aid in the assessment of both cerebrovascular reactivity status and cerebrospinal compensatory reserve, respectively. PRx reflects the ability of the vascular smooth muscle to respond to changes in transmural pressure and is used as a surrogate index of autoregulation. PRx is calculated as a moving correlation coefficient between the slow waves of ICP and ABP on a 5-minute sliding window. A positive PRx (> 0.3) is known to be associated with an unfavorable outcome following TBI.

The RAP, where R represents the correlation coefficient; A, the amplitude; and P, the mean pressure) index represents the dynamic pressure-volume relationship inside the cerebrospinal space, indicating whether the compensatory reserve is intact or exhausted. RAP can be calculated in a similar way as PRx, i.e., as the Pearson’s moving correlation coefficient between changes in amplitude and mean ICP. An RAP around 0 at low ICP (< 15 mm Hg) indicates good cerebrospinal compensatory reserve, whereas RAP close to +1 indicates an exhausted compensatory reserve. Lower RAP values (i.e., negative values) at increased ICP (> 20 mm Hg) are associated with unfavorable outcome in TBI patients, indicating terminal cerebrovascular derangement.

Due to the similarities between ICP and ISP, the PRx and RAP indices might also be used to assess SCI in the same way that they are used in TBI, potentially providing some useful indications concerning autoregulation and compensatory reserve.

Using the same methodology, the equivalent indices are now called spinal PRx (sPRx) and spinal RAP (sRAP). To calculate sPRx, instead of correlating ABP and ICP, we substitute the latter with ISP. Thirty consecutive 10-second averages of ISP, ABP, and the pulse amplitude of ISP are taken to calculate the moving correlation coefficients within a 5-minute window. We hypothesized that sPRx would indicate intact or disturbed cerebrospinal reactivity, showing negative or positive values, respectively, and that the status of the local spinal compensatory reserve at the injury site of a TSCI could be described by the sRAP index.

## Results

**Morphology of the Peaks of the ISP Pulse Waveform**

Analogous to ICP, 3 peaks appear in the ISP pulse waveform—P1, P2, and P3—as demonstrated in Fig. 1. P1 is associated with the systolic peak of ABP, representing the percussion wave. P2 corresponds to intraspinal compliance, representing the tidal wave. P3 is linked to aortic valve closure and the dicrotic wave subsequent to the dicrotic notch of arterial pulsation.

Elevation of the mean ISP alters the shape of the pulse waveform: as ISP starts to increase, P2 also rises with the pulse waveform, acquiring a round shape due to the superimposition of P1 and P2; the difference between them becomes hardly recognizable (Fig. 1A). As ISP continues to increase, P2 rises further to become clearly distinguishable on the pulse waveform at the level above P1 and P3 (Fig. 1B). At very high ISP, there is a disproportionate elevation of P2 and P3, with the pulse waveform acquiring a triangular or pyramidal shape where P2 is dominant and P1 is hardly visible (Fig. 1C).

**Time and Frequency Domains**

The ISP waveform contains 3 wave components that overlap in the time domain. Corresponding spectral analysis of the frequency domain allows the separation of these components, which can be identified as slow, respiratory, and pulse waves (Fig. 2). Slow waves are present at low frequencies (0.05–0.0055 Hz, or in periods of 20 seconds to 3 minutes), whereas respiratory waves are related to the frequency of the respiratory cycle at 0.13–0.3 Hz or 8–20 cycles/minute. The pulse waves consist of different harmonics, with the first harmonic denoted as the fundamental component corresponding to the frequency equal to a heart rate (~1 Hz), while higher peaks in the frequency domain are considered higher harmonics.

**Relationship Between Mean ISP and Its Amplitude**

A typical trend for the relationship between mean ISP and its fundamental harmonic amplitude (II) is presented in Fig. 3 as a long-term recording from a single patient. The 2 parameters—ISP and II—demonstrate a positive and direct relationship, and increasing ISP leads to increases in II. These proportional changes are similar to the ones described for the pulse amplitude of ICP caused by changes in mean ICP.

The relationship between ISP and II is described by the time domain of the sRAP index, which can express the status of the spinal compensatory reserve: the example in Fig. 4 demonstrates the continuous 5-day monitoring of ISP and II, with sRAP fluctuating from periods of low (~0) to high (~1) values, thereby signifying periods where pressure-volume compensation is normal or impaired, respectively.

**Slow ISP Waves and Interaction With ABP**

The interaction between the slow fluctuations of ABP and ISP is expressed by the sPRx index, the values of which can be indicative of the spinal vascular reactivity capacity. This capacity can be monitored, with the exam-
ple included in Fig. 5 depicting long-term fluctuations in sPRx. In the beginning, sPRx is unstable and varies from highly positive to highly negative, but after the middle of the recording period it becomes stable and positive (> 0.4), thereby signifying impaired reactivity.

The examples in Fig. 6 demonstrate 2 contrasting cases of spinal reactivity capacity. In Fig. 6 left, sPRx is low and negative, indicating an inverse relationship between changes in ABP and ISP, and thus the presence of pressure reactivity. In contrast, Fig. 6 right depicts a highly positive sPRx, denoting a positive and passive relationship between ABP and ISP, therefore characterizing a depleted reactivity reserve.

Relationship Between sPRx and SCPP

Based on the similarities with PRx in terms of pressure reactivity, sPRx may as well characterize the equivalent spinal autoregulatory capacity. For this reason, we sought

FIG. 1. ISP pulse wave consists of 3 main components represented by 3 peaks: the percussion wave (P1); the tidal wave (P2); and the dicrotic wave (P3). The morphological shape of the ISP pulse wave is altered with different levels of ISP. A: Increased ISP results in an increased P2, which becomes superimposed with P1 and results in a round ISP waveform. B: ISP at a higher level has a clearly distinguishable P2 that is higher than the P1 and P3 levels. C: At very high ISP, the pulse wave acquires a triangular shape, and P2 becomes dominant and P1 becomes less visible.

FIG. 2. Signal analysis of ISP in the time and frequency domains of a patient’s recording. Spectral analysis of ISP demonstrates slow vasogenic waves at a low frequency, followed by respiratory waves and pulse waves at a higher frequency. The pulse waves consist of multiple harmonics, with the fundamental harmonic (1st harmonic) appearing at a frequency equivalent to a heart rate, followed then by second and third harmonics. A similar effect can be seen in higher harmonics of the respiratory wave.
to explore its relationship with SCPP. A typical example is shown in Fig. 7, where the plot between the 2 parameters shows a U-shaped curve. This relationship illustrates that spinal autoregulation becomes worse at both low and high SCPP, as indicated by high sPRx at both occasions. The middle part of the curve signifies the optimum SCPP range for the best spinal autoregulation, which is based on low sPRx values. The lowest sPRx value indicates optimal SCPP.

**Relationship Between Subdural and Extradural Pressure**

Simultaneous monitoring of both subdural and extradural pressure allowed observational comparison of pressures at both sides of the dura mater (Fig. 8). Extradural pressure demonstrates similar behavior as ISP, however with some notable differences: 1) overall, extradural pressure is lower than ISP, with the difference being in the range of 2–3 mm Hg as shown by the particular example in Fig. 8; 2) extradural pressure pulsatility seems to be lower than ISP with a smaller peak-to-peak amplitude; 3) extradural pressure demonstrates similar fluctuations to ISP, however the magnitude of the slow waves is visibly smaller. Overall, these remarks denote the buffering role of the dura, with the characteristics of extradural pressure being similar, but attenuated, in comparison with the characteristics of ISP.

**Discussion**

The first paper to describe ISP recordings was recently published, with the use of a microsensor inserted in the operating room allowing continuous and reliable ISP recordings that lasted up to a few days. This new and promising technique has allowed us to observe in close detail the morphology of the ISP pulse waveform and its different wave components.

The ISP waveform resembles the respective ICP wave-
form, which is formed by the superimposition of the pulse components (P1, P2, and P3 peaks) and is synchronized with arterial pressure. The proportions between P1 and P2 vary, but the general trends indicate that as mean ISP increases, P2 becomes dominant and increases above P1. In some cases, this increase in P2 first causes the pulse wave configuration to acquire a round shape, with a further increase in mean ISP resulting in a triangular shape that is characteristic of both high ICP and ISP. On ICP analysis, the behavior of P2 has been known to depend on cerebral compliance, with the rise in ICP resulting in a reduction in compliance and a rise in P2.\textsuperscript{5} After TSCI, swelling of the injured cord results in obliteration of the subarachnoid space for CSF at that level, which is associated with a significant increase in ISP at the injury site\textsuperscript{25} because the lack of distensibility of the dura makes it unable to compensate for the expansion of the spinal cord tissue, like in an injured brain with brain edema. Therefore, further increases in ISP reduce spinal compliance, as reflected in a rise in P2.

Spectral analysis of the ISP signal revealed a frequency composition of ISP that is analogous to ICP, with the presence of slow, respiratory, and pulse waves. The pulse waves consist of multiple harmonics, with the fundamental harmonic amplitude of ISP at the heart rate frequency being proportional to the changes in the mean ISP value. This proportionality may suggest that the spinal pressure-volume relationship is exponential\textsuperscript{2,17}—similar to the cranial compartment—and a characterization of both the elastance of the cerebrospinal space and the transmission of arterial pulsations to the CSF compartment.\textsuperscript{4}

The sRAP index, as an equivalent of RAP, denotes the degree of correlation between mean ISP and its amplitude in short periods of time and can indicate the working point in the exponential pressure-volume curve. An sRAP close to 0 indicates a lack of synchronization between changes in the mean ISP and its amplitude, signifying a good compensatory reserve at low ISP, whereas a change in volume produces no or very little change in pressure. In contrast, as sRAP increases toward a value of +1, a direct relationship between mean ISP and its amplitude is established. This is indicative of the passive association of changes between mean ISP and its amplitude and an impaired compensatory reserve, where a further change in volume cannot be compensated and will cause an increase in ISP.

In TBI, the association between the slow fluctuations of ABP and ICP, as expressed by the PRx index, can characterize the autoregulatory status of the cerebrovascular bed. Similarly, in SCI, the equivalent sPRx index can be cal-

![Figure 5](image1.png)

**FIG. 5.** Time series of ABP and ISP measurements in a recording of a single patient. The relationship between ABP and ISP can be depicted using the spinal pressure reactivity index (sPRx), which can present a measure of spinal vascular reactivity: 0 or negative sPRx indicates normal reactivity, whereas positive sPRx (> 0.3) can signify an impairment in the capacity of the vessels to react to changes in pressure.

![Figure 6](image2.png)

**FIG. 6.** Examples of assessing sPRx through the relationship between slow waves, ABP, and ISP in 2 different patients. **Left:** Most of the time sPRx is below 0, indicating an inverse relationship between ABP and ISP and signifying the reactivity of the vascular bed to changes in pressure. **Right:** sPRx is highly positive, demonstrating a passive and direct relationship between ISP and ABP and signifying impaired spinal vascular reactivity.
calculated using ABP and ISP measurements to specify the spinal vascular reactivity, which could be associated with the equivalent autoregulatory capacity for supplying blood to the spinal cord. Our recordings present long-time fluctuations in sPRx (Fig. 5) with periods of active spinal pressure reactivity where changes in ABP were compensated and rendered a negative sPRx (Fig. 6 left), or impaired reactivity where changes in ABP were passively transmitted to ISP and thereby rendered a positive sPRx (Fig. 6 right).

The relationship between sPRx and SCPP can reveal important aspects regarding how autoregulation is associated with the blood supply to the spinal cord. Both hypoperfusion and hyperperfusion could be linked with impaired spinal autoregulatory capacity, as shown by the U-shaped curve of sPRx plotted against SCPP (Fig. 7) which indicates that nonreactive vessels are unable to provide adequate perfusion to the spinal cord. Through this relationship, the optimum SCPP value for the management of TSCI patients could be characterized by the minimum sPRx. Likewise, according to TBI analysis and PRx, the philosophy behind calculating the “optimal SCPP” is that the minimum sPRx would indicate the specific point at which pressure reactivity is most effective. In that way, optimal SCPP could also be applied to TSCI patients, with adjustment of SCPP to its indicated optimal value providing adequate levels of perfusion to the spinal cord. Optimal SCPP should be individually calculated for each specific patient, as patterns of injury are highly variable and thus one SCPP threshold cannot be optimally applied to all patients, as is the case for TBI patients.1,24

**Fig. 7.** Relationship between SCPP and sPRx in a patient after spinal cord injury. When plotted together, the relationship between sPRx and SCPP demonstrates a U-shaped curve, with autoregulatory capacity becoming worse at both low and high SCPP and optimal SCPP indicated by the lowest sPRx value.

**Fig. 8.** Simultaneous monitoring of both subdural ISP and extradural pressure. Extradural pressure demonstrates similar behavior to ISP; however, extradural pressure appears to demonstrate overall lower values and slow waves of a smaller magnitude in comparison with ISP, possibly demonstrating a buffering role by the dura mater.
In head injuries, a large difference between actual CPP and the optimal CPP value is thought to play an important role in terms of outcome: patients with significantly lower or higher CPP than the indicated optimal level demonstrate less favorable outcomes after TBI. A future study focusing on optimal SCPP and outcomes could confirm if this also applies to TSCI patients.

Limitations

The small number of patients who received ISP monitoring is a limitation of this study. Even though strong similarities are present between morphology and waveform analysis of ICP and ISP, a larger amount of data are required to potentially establish a subsequent link of ISP, SCPP, and their derived indices sRAP and sPRx with functional outcome following spinal cord injury. However, the purpose of this study was observational and to provide a qualitative illustration of ISP characteristics using more detailed continuation of our previous study. In terms of ICP monitoring, supratentorial pressure gradients may exist. Similar gradients may exist in ISP. Therefore, it is likely that the pressure measured within nonswollen sections of the spinal cord is much lower or even nearly normal. This is something that should be examined in future studies.

Conclusions

This preliminary study suggested that the methodology for analyzing the ICP waveform may be transformed to analyzing the ISP waveform, and the observational results indicated the morphological and spectral similarities between ISP in spinal cord injury and ICP recorded in TBI. More studies on this topic are needed to verify the clinical feasibility of applying the known methods of ICP waveform analysis, such as the indices of compensatory reserve and autoregulation, in patients with TSCI.

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Author Contributions

Conception and design: Papadopoulos. Acquisition of data: Werndle, Phang, Saadoun, Zoumprouli, Papadopoulos. Analysis and interpretation of data: Varsos. Drafting the article: Varsos. Critically revising the article: Werndle, Z Czosnyka, Smielewski, Kolias, Phang, Saadoun, Bell, Zoumprouli, Papadopoulos, M Czosnyka. Reviewed submitted version of manuscript: Z Czosnyka, Smielewski, M Czosnyka. Approved the final version of the manuscript on behalf of all authors: Varsos. Administrative/technical/material support: Werndle, Smielewski, Phang, Saadoun, Zoumprouli. Study supervision: Papadopoulos, M Czosnyka.

Correspondence

Georgios V. Varsos, St Edmund’s College, University of Cambridge, Cambridge, CB3 0BN, United Kingdom. email: gv249@cam.ac.uk.