Effect of position on intracranial pressure and compliance:

cross-sectional study including 101 patients

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Key words

Cerebrospinal fluid dynamics

Intracranial compliance

Intracranial pressure monitoring

Intracranial pressure waveform

Pulse amplitude

Funding

No funding was received for this research.

Previous presentations

Portions of this work were presented in abstract and oral presentation form at the Society of British Neurological Surgeons & Association of British Neurologists joint meeting (London, 2018), the 10th Meeting of the International Society for Hydrocephalus and Cerebrospinal Fluid Disorders (Bologna, 2018) and the 11th Meeting of the International Society for Hydrocephalus and Cerebrospinal Fluid Disorders (Vancouver, 2019).

Clinical article for Journal of Neurosurgery

Abstract word count: 364 words

Text word count: 3507 words

Number of references: 21

Number of tables and/or figures: 7

Abstract

Objective

A better understanding of the effect of position on intracranial pressure (ICP) and compliance is important for the development of treatment strategies that can restore the normal cerebrospinal fluid (CSF) dynamics. There is limited knowledge of the effect of position on intracranial compliance. In this cross-sectional study we tested the association of pulse amplitude with position and day/night cycle. Additionally, we describe the postural ICP and pulse amplitude changes of patients with 'normal' ICP dynamics.

Methods

This single-centre retrospective study included patients with suspected/confirmed CSF dynamics abnormalities who were investigated with elective 24-hour ICP monitoring between October 2017 and September 2019. Patients were enrolled in a short exercise battery including 4 positions: supine, lumbar puncture position in left lateral decubitus, sitting and standing. Each position was maintained for 2 minutes, mean ICP and pulse amplitude were calculated for each position. 24-hour, day and night median ICP and pulse amplitude data were also collected. Linear regression models were used to test the correlation of pulse amplitude with position and day/night cycle. All linear regressions were corrected for confounders. The postural ICP monitoring results of patients without obvious ICP dynamic abnormality were summarised.

Results

101 patients (24 males and 77 females) with a mean age of 39 years (±13SD), were included in the study. The adjusted linear regression models demonstrated a significant association of ICP with position and day/night cycle, resulting in upright (sitting and standing) and day ICP being lower than supine/night ICP values. The adjusted linear regression model was also significant for the association of pulse amplitude with position and day/night cycle, resulting in upright and day pulse amplitude being higher than supine/night pulse amplitude results. These associations were confirmed for patients with and without shunts. Patients without clear ICP dynamics abnormality had a tighter control of the postural ICP changes compared to the other patients, however, the difference between groups was not statistically significant.

Conclusions

This is the largest study investigating the effect of postural changes on intracranial compliance. The results of this study suggest that pulse amplitude (as well as ICP) is significantly associated with posture, increasing in upright positions compared to supine. Further studies will be needed to investigate the mechanism behind this association.

Introduction

In recent years, ICP monitoring has gained an important role in the diagnosis and treatment of patients affected by chronic cerebrospinal fluid (CSF) dynamics disturbances as, for example, normal pressure hydrocephalus (NPH), idiopathic intracranial hypertension (IIH), Chiari malformation I and various forms of hydrocephalus [1]. Compared to patients in the acute setting, patients with chronic CSF dynamics disorders are most commonly mobile and provide the unique opportunity to study the changes of ICP and pulse amplitude in different body positions.

Most studies on ICP monitoring describe ICP in the supine position, despite the fact that humans spend most of their time in an upright posture. A better insight into the effect of position on ICP and compliance is important for several reasons. First of all, compared to other fields, the available knowledge on ICP physiology is limited and this is probably due to the invasive nature of the investigations needed to measure this important physiological parameter. More importantly, our treatments may not be able to restore the physiological CSF dynamics until we know how they work. Previous studies have demonstrated that ICP is lower in upright position compared to supine [2-7]. A better understanding of the effect of position on ICP dynamics could also allow the improvement of CSF shunt technologies towards the creation of the long-awaited 'smart shunt system' [8].

Intracranial compliance is the ability of the intracranial compartment to accommodate an increase in volume without a large increase in ICP. Pulse amplitude (the difference between systolic and diastolic ICP) is considered a reliable indirect marker of compliance: the higher the pulse amplitude, the lower the brain compliance. Intracranial compliance is recognised to be a very

useful marker in clinical practice [1], however, the effect of position on markers of intracranial compliance is not clear. For example, Farahmand *et al.* noticed slightly higher ICP waveform amplitude (indicating lower brain compliance) in the upright posture compared to supine [5]. In contrast, Raabe *et al.* analysed markers of intracranial compliance in 13 patients with intraventricular sensors and concluded that different levels of head-up tilts do not affect intracranial compliance [9]. Non-invasive studies using MRI imaging or mathematical models have concluded that brain compliance is increased in the upright position compared to supine [10,11].

The intracranial compliance model proposed by Marmarou in 1975, demonstrates that higher ICP levels correspond to lower intracranial compliance [12]. Since supine position is associated with higher ICP levels, we hypothesised that intracranial compliance would be reduced in this position compared to upright posture. The specific aims of this cross-sectional study were:

1. to test the hypothesis that pulse amplitude (as a marker of intracranial compliance) is correlated to body position;
2. to test the hypothesis that pulse amplitude is correlated to the day/night cycle, since night ICP is recorded in supine position, while day ICP is mostly measured in an upright position;
3. to describe the mean ICP and pulse amplitude in different body positions for patients considered to have 'near-normal' ICP dynamics based on a post-hoc analysis.

Methods

This is a single centre cross-sectional study conducted at the National Hospital for Neurology and Neurosurgery (NHNN, London, UK) between October 2017 and September 2019. This study has been approved by the North East-Newcastle & North Tyneside 2 Research Ethics Committee and the Health Research Authority (20/NE/0127). Due to the study design (retrospective analysis) written consent was waived.

Patients with suspected or confirmed CSF dynamics disturbances (e.g. IIH, CSF leaks, hydrocephalus, Chiari malformation I) who underwent elective ICP monitoring were included if meeting the following eligibility criteria: (i) complete 24-hour ICP monitoring data available, (ii) ICP monitoring performed through intraparenchymal sensor (non-telemetric) and (iii) completion of short exercise battery during ICP monitoring period under the supervision of one of the authors (LD). Patients were identified through screening of the local clinical ICP monitoring database.

ICP monitoring method

In our institution, patients are considered for ICP monitoring only when affected by signs and symptoms consistent with altered CSF dynamics, in whom other less invasive or non-invasive investigation methods were inconclusive. The clinical indication for elective 24-hour ICP monitoring was agreed by a multidisciplinary team including neurosurgeons, neurologists and ophthalmologists. These multidisciplinary discussions occur on a case-by-case basis, the clinical conditions that are considered are intractable headaches due to suspected CSF dynamics disturbance, IIH, Chiari malformation type I, spontaneous intracranial hypotension, CSF leaks (to investigate if driven by high ICP), hydrocephalus, shunt-dependent patients with suspected shunt

malfunctions/blockage. An intraparenchymal ICP probe was inserted in the operating theatre, under sedation or local anaesthesia, in the right frontal area. One of the following two types of ICP probes was chosen depending on the surgeon's preference: Spiegelberg parenchymal probe with cranial bolt (Spiegelberg GmbH & Co KG, Hamburg, Germany) or Raumedic Neurovent-P (Raumedic AG, Helmbrechts, Germany). The monitoring was performed for a period of 24 hours [13]. In order to match their usual level of activity, patients were encouraged to sit, stand and walk during the daytime and rest supine in bed overnight. Raw ICP data was collected through a bedside monitor at a sampling frequency of 100 Hz and then analysed through the ICM+ software (University of Cambridge Enterprise Ltd). The final ICP monitoring results are summarised as median ICP and median pulse amplitude over 24 hours, day (12:00 - 18:00) and night (00:00 - 06:00). The pulse amplitude is used as a marker of brain compliance [14]. Further details on this ICP monitoring method have been described previously elsewhere [13,15].

Short exercise battery

During the 24-hour ICP monitoring period, the patients underwent a short exercise battery under the supervision of one of the authors (L.D.). This short exercise battery is part of the standard of care for ICP monitoring in our institution. The patients were asked to assume the following 4 positions: (i) supine in bed (with one pillow under the head), (ii) lumbar puncture position in lateral decubitus (lying on the left side with flexed hips and knees and one pillow under the head), (iii) sitting at the edge of the bed, (iv) standing. Start and stop times for each position were marked using the ICP monitor time stamp (hh:mm:ss format). The positions were performed in the described order and each of them was maintained for 2 minutes once the ICP steady state was confirmed. Stabilisation of the ICP in each position was sought and ascertained through the direct

observation of the ICP trace on the bedside monitor. Recordings were discarded and repeated if the patient coughed, sneezed or talked during the exercise battery. Two-minute mean ICP and pulse amplitude for each of the positions was calculated.

Variables

Information on the patients' demographic characteristics, indications for ICP monitoring and previous treatments (e.g. presence and components of a CSF diversion shunt) was retrospectively retrieved. The following ICP monitoring results were recorded: median ICP and pulse amplitude (24-hour, day and night), mean 2-minute ICP and pulse amplitude during each of the 4 exercise battery positions. All ICP and pulse amplitude values are expressed in mmHg.

Statistical analysis

Considering the structural differences between Spiegelberg and Raumedic ICP sensors, all results were stratified by type of sensor. Linear regression models were used to test the effect of position (independent variable) on mean pulse amplitude and ICP (dependent variables). Additionally, linear regression models were used to test the effect of the day/night cycle (independent variable) on median pulse amplitude and ICP (dependent variables). All analyses were stratified by type of sensor and also adjusted for the following confounding variables: age, sex, patient identification number, indication for ICP monitoring and ICP/pulse amplitude. Separate regressions models were built for patients with pre-existing CSF diversion shunts at the time of ICP monitoring.

Patients were further categorised into one of three subgroups for further analysis: (a) 'normal' ICP monitoring results, (b) 'abnormal' ICP monitoring results, and (c) 'shunted' patients (grouped

separately regardless of their ICP monitoring results). The 'normal' group included non-shunted patients complaining of intractable headaches who were suspected to have CSF dynamics abnormalities (e.g. IIH), but did not present any evident abnormality in their ICP monitoring results and did not proceed to further neurosurgical input. The 'abnormal' group consisted of non-shunted patients considered to have abnormal ICP monitoring results requiring treatment or further neurosurgical investigations. The 'shunt' group consisted of patients with a CSF diversion shunt at the time of ICP monitoring. Interpretation of the ICP monitoring results and management decisions were conducted by the multidisciplinary team who were not aware of the results of the exercise battery. The parameters used to interpret the ICP monitoring results included median ICP (over 24 hours, during the day and night), median PA (over 24 hours, during the day and night), peak/trough ICP, number of ICP spikes above 25 mmHg, percentage of time the ICP was negative or above 15 mmHg, ICP frequency distribution histogram and Pearson coefficient of correlation between ICP/PA. These parameters were used to establish whether CSF dynamics abnormalities were present and make decisions on optimal management methods (e.g. surgical treatment, shunt setting adjustment). Further information on the local ICP monitoring protocol have previously been published [15].

Due to the exploratory nature of the study a formal sample size calculation was not performed, and all eligible patients were included in the study. Continuous variables were summarised as means (standard deviation) and categorical variables as percentages. A significance level 0.05 was used. Microsoft® Excel for Mac (version 16.25), Stata© (version 15.0) and GraphPad Prism for macOS (version 8.4.1) were used for the data collection and statistical analysis.

Results

Between October 2017 and September 2019, 264 patients underwent elective ICP monitoring at the NHNN. Of these, 101 met the eligibility criteria and were included in the study. **Table 1** describes the patients' baseline characteristics and the clinical indications for ICP monitoring.

Effect of position on ICP and pulse amplitude in patients without shunts

An example of the ICP monitoring recording during the short exercise battery is displayed in **Figure 1**. **Table 2** summarises the 24-hour and exercise battery ICP monitoring results for the 68 patients without shunts. Compared to supine position, patients had a higher ICP in lumbar puncture position (average difference 3.8±4.2 mmHg) and a lower ICP in sitting and standing positions (average differences 8.6±4.8 mmHg and 9.3±4.6 mmHg respectively) (**Figure 2**). The unadjusted linear regression models demonstrated a significant correlation between ICP (dependent variable) and all body positions (independent variable) with both Raumedic (adjusted R^2=0.3, $F(3,104)=16.5$, $p<0.05$) and Spiegelberg (adjusted R^2=0.39, $F(3,159)$, $p<0.05$) ICP monitors. The correlation was also statistically significant in the adjusted multiple regression models ($p<0.05$ for all positions for both Raumedic and Spiegelberg ICP monitors).

Compared to supine position, pulse amplitude was slightly higher in lumbar puncture, sitting and standing positions (see **Table 2**). In the unadjusted linear regression models, this difference achieved statistical significance only with sitting position when Spiegelberg monitors were used. However, when the models were corrected for confounders in the adjusted multiple regressions, pulse amplitude was significantly higher in sitting and standing positions for both Spiegelberg and Raumedic monitors (**Table 3**).

Effect of position on ICP and pulse amplitude in patients with shunts

Thirty-three patients had a shunt in situ at the time of ICP monitoring. Also in this group, compared to supine position ICP was higher in lumbar puncture position (average difference 4.9±4 mmHg) and lower in sitting and standing position (average differences 10.6±4.9 mmHg and 12.2±4.7 mmHg respectively). Compared to supine position, pulse amplitude was higher in lumbar puncture, sitting and standing positions (average differences 0.7±2.4 mmHg, 0.7±1.9 mmHg and 0.2±2.2 respectively). Adjusted multiple regression models revealed a significant association between pulse amplitude (dependent variable) and sitting/standing position ($p<0.05$) for both Raumedic and Spiegelberg ICP monitors (see **Table 3**).

A curve of best fit analysis suggests that at extremely low ICP levels (<-10 mmHg), pulse amplitude tends to slightly increase, a situation that most commonly occurs when the patient is in a sitting or standing posture (**Figure 3**).

Effect of day/night cycle on ICP and pulse amplitude in patients without shunts

Compared to daytime, the median night ICP was higher and the median night pulse amplitude was lower (**Table 2**). Adjusted multiple regression models, confirmed a significant association of ICP and pulse amplitude with the day/night cycle. In particular, night ICP was higher than day ICP with both Spiegelberg ($\beta=6.9$, 95% CI 5.1 to 8.8, $p< 0.001$, adjusted $R^2=0.64$) and Raumedic monitors ($\beta=8.3$, 95% CI 6.2 to 10.5, $p<0.001$, adjusted $R^2=0.75$) (**Figure 4A and 4C**). β is used to indicate the slope coefficient of the linear regression analysis. Night pulse amplitude was lower than day pulse amplitude with both Spiegelberg ($\beta=-2.1$, 95% CI -2.9 to -1.4, $p<0.001$, adjusted

R^2=0.50) and Raumedic monitors (β=-3.8, 95% CI -5.1 to -2.6, p<0.001, adjusted R^2=0.65) (**Figure 4B and 4D**).

Effect of day/night cycle on ICP and pulse amplitude in patients with shunts

The adjusted regression models for the 33 patients with shunts in situ demonstrated a significant association between ICP with day/night cycle for both types of monitors, with night ICP being higher than day ICP (Spiegelberg β=5.3, 95% CI 3.2 to 7.5, p<0.001, adjusted R^2=0.48; Raumedic β=9.3, 95% CI 4.4 to 14.2, p=0.001, adjusted R^2=0.45). A significant association was also found between PA and day/night cycle, with day pulse amplitude being higher than night pulse amplitude (Spiegelberg β=-1.2, 95% CI -2.2 to -0.2, p=0.018, adjusted R^2=0.10; Raumedic β=-3.5, 95% CI -5.9 to -1, p=0.008, adjusted R^2=0.38).

Subgroup analysis of ICP monitoring results in 'normal', 'abnormal' and 'shunt' groups

The multidisciplinary team interpreted the ICP monitoring results as 'normal' in 20 patients, 'abnormal' in 44 patients and 37 patients had a shunt in situ at the time of ICPM monitoring (‘shunt’ group). During the exercise battery, patients considered to have ‘normal’ ICP monitoring results had the following mean ICP values: mean supine ICP of 7.2 (3.2 SD) mmHg, mean lumbar puncture position ICP of 10.5 (3.5 SD) mmHg, mean sitting ICP of -1.4 (4.1 SD) mmHg and mean standing ICP of -1.9 (3.2 SD) mmHg. The mean pulse amplitude results in the ‘normal’ group were: 5.3 (2.1 SD) mmHg in supine position, 5.9 (2.2 SD) mmHg in lumbar puncture position, 6.1 (1.6 SD) in sitting position and 6.2 (1.6 SD) in standing position. There was a tendency for patients in the ‘normal’ group to have smaller changes in ICP when changing body position compared to

the ‘abnormal’ and ‘shunt’ groups; however, the amount of change in ICP was not statistically different among the three groups (Kruskal-Wallis H Test, $p>0.05$ for all positions).

Discussion

This cross-sectional study investigated the effect of position on ICP and pulse amplitude measurements in 101 patients with suspected CSF dynamics disorders. Our results confirmed previous findings suggesting a strong association between position and ICP [2-7]. In addition, we found that pulse amplitude (a marker of intracranial compliance) is also correlated to posture. Contrary to our initial hypothesis, pulse amplitude was higher in sitting and standing postures compared to supine position indicating a slight drop in intracranial compliance when the patients were upright. The investigation of the effect of the day/night cycle on ICP dynamics generated analogous results, with ICP significantly higher during the night (when patients are supine) and pulse amplitude significantly higher during the day (when patients spend most of their time upright). Additionally, the increase in pulse amplitude for upright postures and daytime was confirmed independently of the presence of a CSF diversion shunt.

The brain compliance model proposed by Marmarou in 1975 predicted that high ICP levels should correspond with lower compliance and therefore higher pulse amplitude of the ICP waveform [12]. ICP drops significantly when moving from supine to upright position, with an average decrease of 9.3 mmHg in this study (**Table 2**). However, this was not accompanied by a reduction in pulse amplitude, indeed there was a slight increase of this marker (average increase of 1 mmHg, see **Table 2**). Similar findings were described by Farahmand *et al.* in 2014, who observed higher pulse amplitudes during sitting and walking compared to supine position in a group of 15 patients affected by communicating hydrocephalus. [5] They reported that the difference between sitting and supine pulse amplitude was not statistically significant and attributed the significative increase of pulse amplitude during walking to the irregular waveform recordings that can affect ICP

monitoring quality during movement [5]. This interpretation is plausible, and we also observed that in some patients the upright ICP trace was 'noisier' even though the patients were sitting (or standing) completely still (**Figure 1**). This explanation might also apply to the finding that pulse amplitude is higher during the day compared to night ICP recordings.

A study by Raabe *et al.* investigated the effect of posture (more specifically head-tilt angles) on intracranial compliance through the use of invasive techniques (intraventricular sensors) in 13 patients [9]. The authors concluded that posture does not change intracranial compliance but rather creates a shift of the pressure-volume curve along the pressure axis, without changing its shape. For these reasons, they suggested that measurements of intracranial compliance should be conducted with the patient in supine position or alternatively corrected for this shift [9]. On the other hand, studies investigating intracranial compliance non-invasively, through the use of brain MRI or mathematical models, have found that intracranial compliance is expected to improve in an upright posture.[10,11] The controversies around the effect of position on intracranial compliance are further proof of the complexity of CSF dynamics.

As recently discussed by Marek and Zofia Czosnyka, the ICP waveform is 'rich in information' but also not easy to analyse. [16] There are limitations to the current ICP monitoring and compliance measurement techniques that could have contributed to these results. Due to their mechanical characteristics, pneumatic ICP measuring sensors have been described as being less reliable for the measurement of intracranial compliance markers.[1] For this reason, we stratified our results by sensor type but despite this, we found a similar trend for pulse amplitude changes with position in both Spiegelberg (pneumatic system) and Raumedic Neurovent-P (strain-gauge sensor).

Additionally, it remains unclear whether time-domain or frequency-domain analysis methods are more reliable for the assessment of intracranial compliance. For this study we used frequency-domain analysis performed through the software ICM+, this type of analysis has been reported to underestimate the ICP pulse amplitude signal compared to time-domain analyses.[17] It is possible that the use of frequency-domain analysis may have played a role in our results, however, this would have presumably affected the analysis of pulse amplitude similarly in all positions. Another limitation is the retrospective nature of the study, however, while the analysis is retrospective the data collection has been performed prospectively as part of our local ICP monitoring protocol. Additionally, having information on the capnography waveform and continuous position monitoring would have been useful for the interpretation of the ICP/PA changes, future prospective studies including this information would be valuable.

The venous system has been demonstrated to have a key role for the postural changes of ICP dynamics. In particular, when moving from supine to upright posture, the internal jugular veins collapse, causing a shift of the hydrostatic indifferent point.[4,10,18] It is possible, that these vascular changes could affect intracranial compliance in upright posture. It should be noted that, our findings are in part in keeping with the observation that at very low ICPs, brain compliance tends to decrease. [19,20]

As discussed, it is difficult to ascertain the true origin of the increase of pulse amplitude in upright posture. Additionally, these pulse amplitude changes are minimal (about 1 mmHg from supine to sitting) and in some patients they may not be clinically relevant. However, this finding may be useful for the interpretation of the ICP monitoring results of patients affected by isolated

compliance abnormalities (e.g. Chiari malformation I and NPH). Additionally, this information is of importance for studies on non-invasive ICP monitoring techniques that use in their estimations ICP waveform analysis of patients in upright posture (e.g. tympanic membrane displacement)[1].

Finally, our study provides information on the ICP and pulse amplitude of patients with no clear abnormality on ICP monitoring results ('normal') in different body postures. Our mean ICP results in supine and upright posture are similar to those described by Andresen *et al.* in 4 'healthy' patients undergoing ICP monitoring after removal of a demarcated, small brain tumour.[21] Additionally we provide data on 'normal' pulse amplitude in different posture that were not previously described. We found that patients with 'normal' ICP tended to have a more stable ICP, with smaller ICP postural changes. This finding is similar to the results of a smaller study by Andresen *et al.*[6] and we are in agreement with their statement that shunts seem to mimic abnormal ICP dynamics instead of restoring normal ICP physiology.

Conclusions

This is the largest study investigating the effect of postural changes on ICP dynamics. The results of this study suggest that pulse amplitude (as well as ICP) is significantly associated with posture, increasing in upright positions compared to supine. Moreover, patients with ‘normal’ ICP monitoring results tend to have a tighter control of their ICP and smaller postural ICP changes.

Financial support

No funding was received for this research.

Disclosures

LD is supported by an NIHR Academic Clinical Fellowship and was the recipient of a research fellowship sponsored by B.Braun. MSM serves on the advisory board for Allergan, Novartis, Eli Lilly, Autonomic Technologies Inc and TEVA and has received payment for the development of educational presentations from Allergan, electroCore, Eli Lilly, Novartis and TEVA. LDW has received honoraria from and served on advisory boards for Medtronic, B.Braun and Codman. AKT research time was supported by the National Institute for Health Research University College London Hospitals Biomedical Research Centre. The other authors have no disclosures to report.

Author contributions

LD and AKT designed and conceptualised the study. LD and CLC acquired the data. LD analysed the data and drafted the manuscript. All the authors interpreted the results and revised the manuscript for intellectual content.

Acknowledgements

We acknowledge Simon D. Thompson, MSc (Victor Horsley Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, London, United Kingdom) and Joana Ramos, BSN (Victor Horsley Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, London, United Kingdom), for their contribution in the collection of the data required for the study. No compensation outside of salary was received.

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Table 1. Patients' characteristics and underlying diagnoses.

Sex	**N (%)**
- Male	24 (24)
- Female	77 (76)
Age (years)	**Mean (SD)**
	39 (13)
Underlying diagnosis at the time of ICP monitoring	**N (%)**
- Diagnosis not yet established	33 (32)
- Hydrocephalus	32 (32)
- Chiari malformation	19 (19)
- Idiopathic Intracranial Hypertension	17 (17)
CSF diversion shunt	**N (%)**
- No shunt	68 (67)
- Ventriculoperitoneal shunt	28 (28)
- Lumboperitoneal shunt	3 (3)
- Other type of shunt	2 (2)
Shunt valve	**N (%)**
- Miethke pro-GAV	12 (37)
- Fixed pressure valve	7 (21)
- Medtronic Strata	5 (15)
- Miethke pro-GAV and pro-SA	3 (9)
- Sophysa Polaris	2 (6)
- Valveless shunt	2 (6)
- Codman Certas	1 (3)
- Codman Hakim	1 (3)
Type of ICP monitor	**N (%)**
- Spiegelberg	61 (60)
- Raumedic Neurovent P	40 (40)
ICP: Intracranial Pressure	

Table 2. Twenty-four-hour and exercise battery intracranial pressure (ICP) monitoring results stratified by type of monitor in patients without shunts

	All (n=68)	**Spiegelberg (n=41)**	**Raumedic (n=27)**
24-hour ICP monitoring results, mean (SD)			
24-hour ICP	6.9 (7.1)	4.6 (6.3)	10.4 (6.8)
24-hour PA	5.9 (2.7)	5.5 (2)	6.5 (3.4)
Day[1] ICP	4.3 (7.1)	2.1 (6.3)	7.7 (6.8)
Day PA	6.3 (2.6)	5.8 (2)	6.9 (3.1)
Night[2] ICP	10.4 (7.2)	7.7 (5.9)	14.5 (7.2)
Night PA	5.4 (2.9)	5.1 (2.1)	5.9 (3.7)
Exercise battery ICP monitoring results, mean (SD)			
Supine ICP	11.2 (6.9)	8.8 (5.7)	14.7 (7.2)
Supine PA	6.4 (3.1)	5.9 (2.8)	7.1 (3.6)
LP position ICP	14.9 (8.9)	12.5 (8.1)	18.5 (9)
LP position PA	7 (3.5)	6.9 (3.7)	7.3 (3.3)
Sitting ICP	2.6 (8.7)	-0.3 (8)	6.9 (8)
Sitting PA	7.5 (3.9)	7.5 (3.9)	7.6 (4)
Standing ICP	2 (7.3)	-0.9 (6.6)	6.3 (6.3)
Standing PA	7 (2.8)	6.8 (2.6)	7.2 (3.2)
ICP and PA differences, mean (SD)			
Night ICP minus day ICP	6.1 (4.6)	5.6 (4.7)	6.8 (4.2)
Night PA minus day PA	-0.8 (1.2)	-0.7 (1.2)	-1 (1.3)
LP position minus supine ICP	3.8 (4.2)	3.7 (4.7)	3.8 (3.5)
LP position minus supine PA	0.6 (3)	0.9 (3.6)	0.1 (1.7)
Sitting minus supine ICP	-8.6 (4.8)	-9.1 (4.9)	-7.8 (4.6)
Sitting minus supine PA	1.1 (2.6)	1.5 (2.9)	0.4 (2)
Standing minus supine ICP	-9.3 (4.6)	-10 (4.5)	-8.4 (4.7)

Standing minus supine PA	0.5 (2.1)	0.8 (2.2)	0.1 (2.0)

ICP: Intracranial Pressure, LP: Lumbar Puncture, PA: Pulse Amplitude, SD: Standard Deviation

[1]Day ICP/PA= median ICP/PA between 12:00 and 18:00 hours

[2]Night ICP/PA= median ICP/PA between 00:00 and 06:00 hours

Table 3. Adjusted multiple regression models testing the association between position and pulse amplitude (PA) stratified by monitor type.

Adjusted multiple regression model testing the association between PA and position in patients without shunts						
PA	**Spiegelberg**			**Raumedic**		
Variables	**Beta**	**p**	**95% CI**	**Beta**	**p**	**95% CI**
LP*	-0.4	0.46	-1.5 to 0.7	-1.3	**0.029**	-2.5 to -0.1
Sitting*	4.7	**<0.001**	3.6 to 5.9	3.4	**<0.001**	2.2 to 4.7
Standing*	4.2	**<0.001**	3.1 to 5.4	3.3	**<0.001**	2 to 4.6
ICP	0.4	<0.001	0.3 to 0.4	0.4	<0.001	0.3 to 0.4
Sex	0.7	0.13	-	2.6	<0.001	-
Age	0.03	0.026	-	0.1	<0.001	-
Indication	0.04	0.84	-	0.5	0.007	-
	Adjusted R^2=0.47			Adjusted R^2=0.61		
Adjusted multiple regression model testing the association between PA and position in patients with shunts						
PA	**Spiegelberg**			**Raumedic**		
Variables	**Beta**	**p**	**95% CI**	**Beta**	**p**	**95% CI**
LP*	-0.3	0.650	-1.5 to 0.9	0.3	0.595	-0.9 to 1.6
Sitting*	2.7	**0.001**	1.2 to 4.2	1.8	**0.012**	0.4 to 3.2
Standing*	2.2	**0.007**	0.6 to 3.8	1.8	**0.014**	0.4 to 3.3
ICP	0.1	0.001	0.1 to 0.2	0.2	<0.001	0.1 to 0.3
Sex	-0.2	0.7	-	-0.5	0.4	-
Age	0.1	0.03	-	-0.1	0.028	-
Indication	0.3	0.23	-	-0.7	0.14	-
	Adjusted R^2=0.16			Adjusted R^2=0.63		
CI: Confidence Intervals, ICP: Intracranial Pressure, LP: Lumbar Puncture position, PA: Pulse Amplitude *Compared to supine position ICP/PA						

Figure 1. Example of intracranial pressure (ICP) monitoring recording during the short exercise battery.100 Hz raw ICP measurements are displayed.

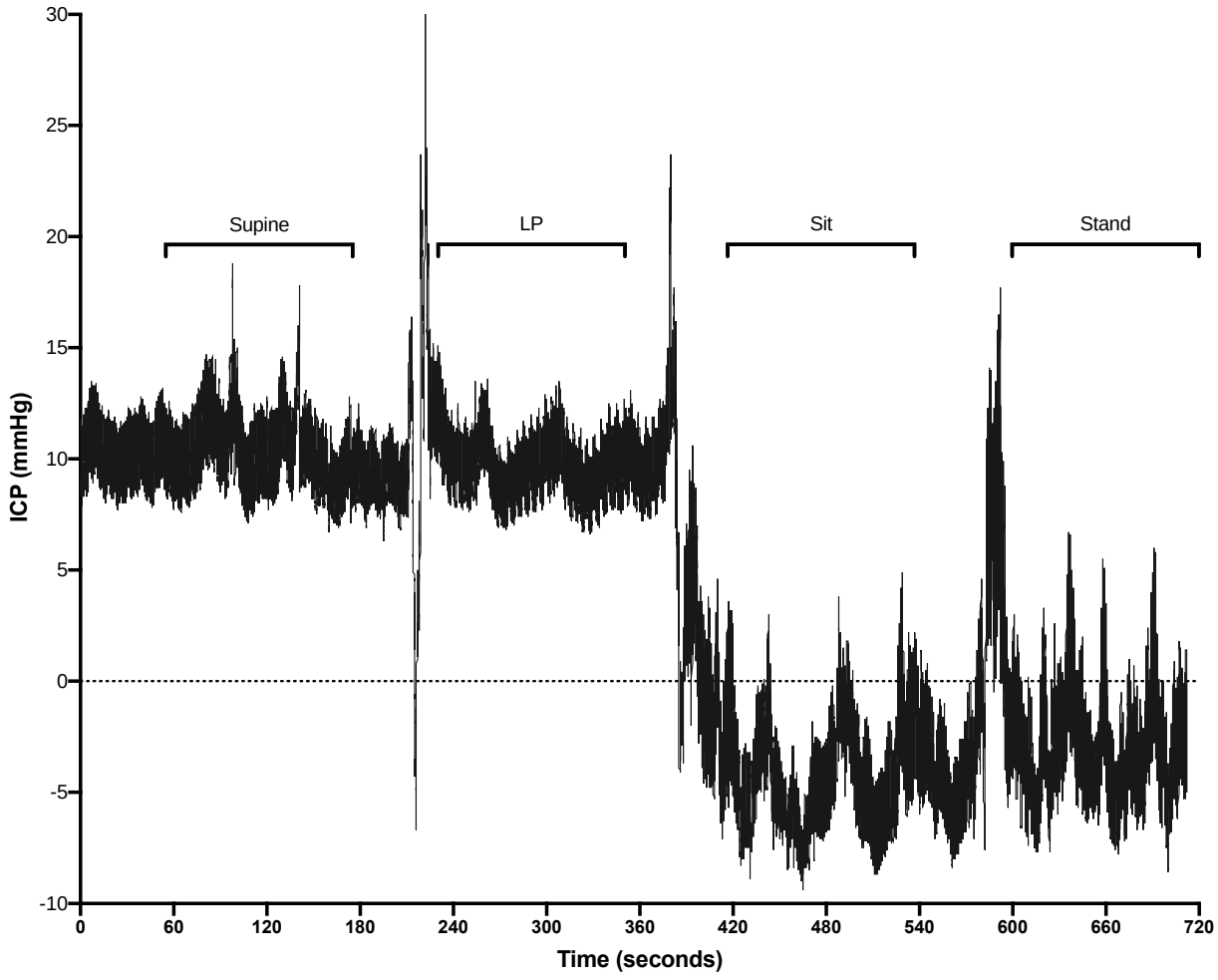


Figure 2. Mean intracranial pressure (ICP) and pulse amplitude (PA) with standard deviations in different body positions stratified by type of ICP monitor (A and B Spiegelberg, C and D Raumedic, only patients without shunts included).

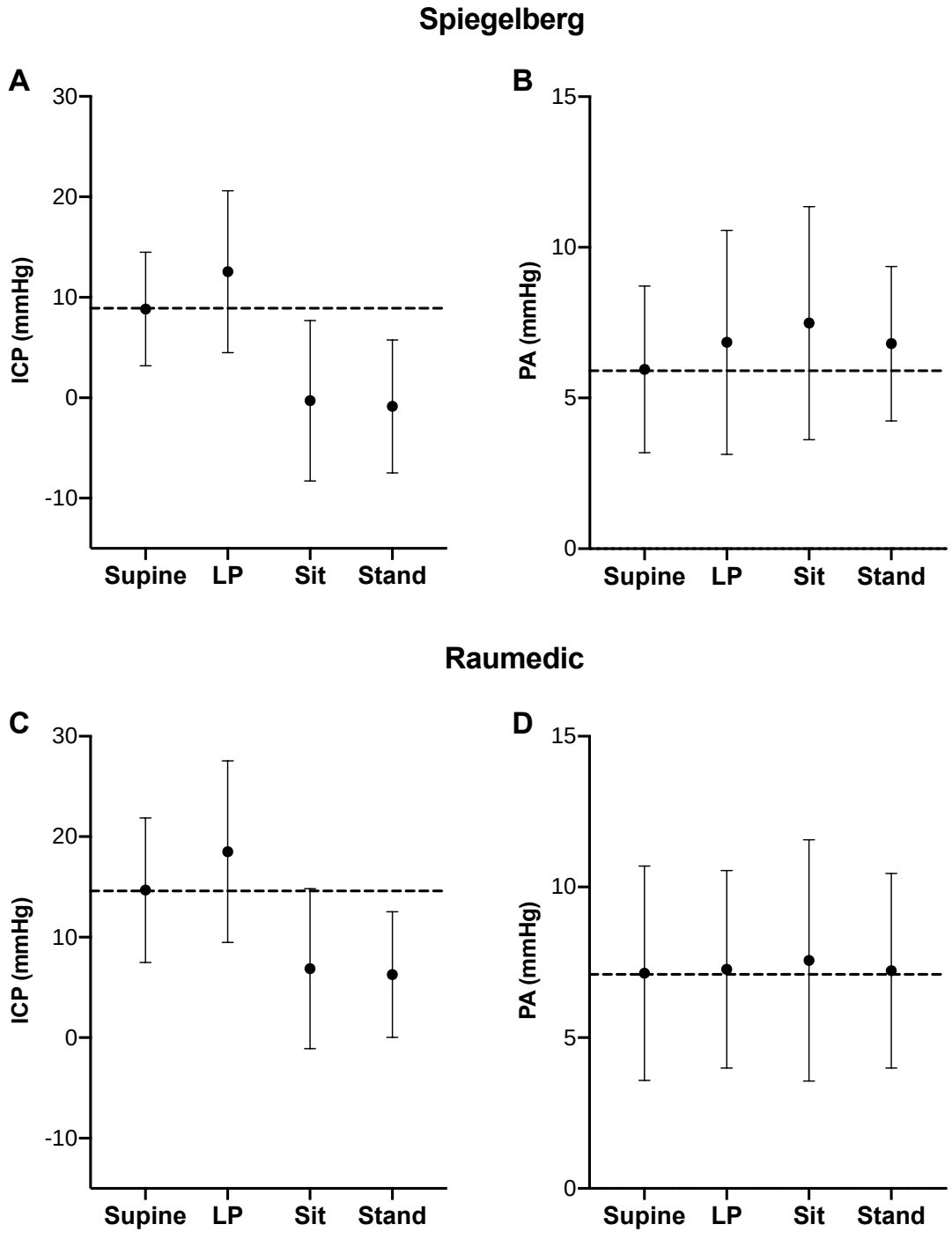


Figure 3. Scatter plot and curve of best fit of pulse amplitude (PA) and intracranial pressure (ICP) measurements in different body positions for 101 patients.

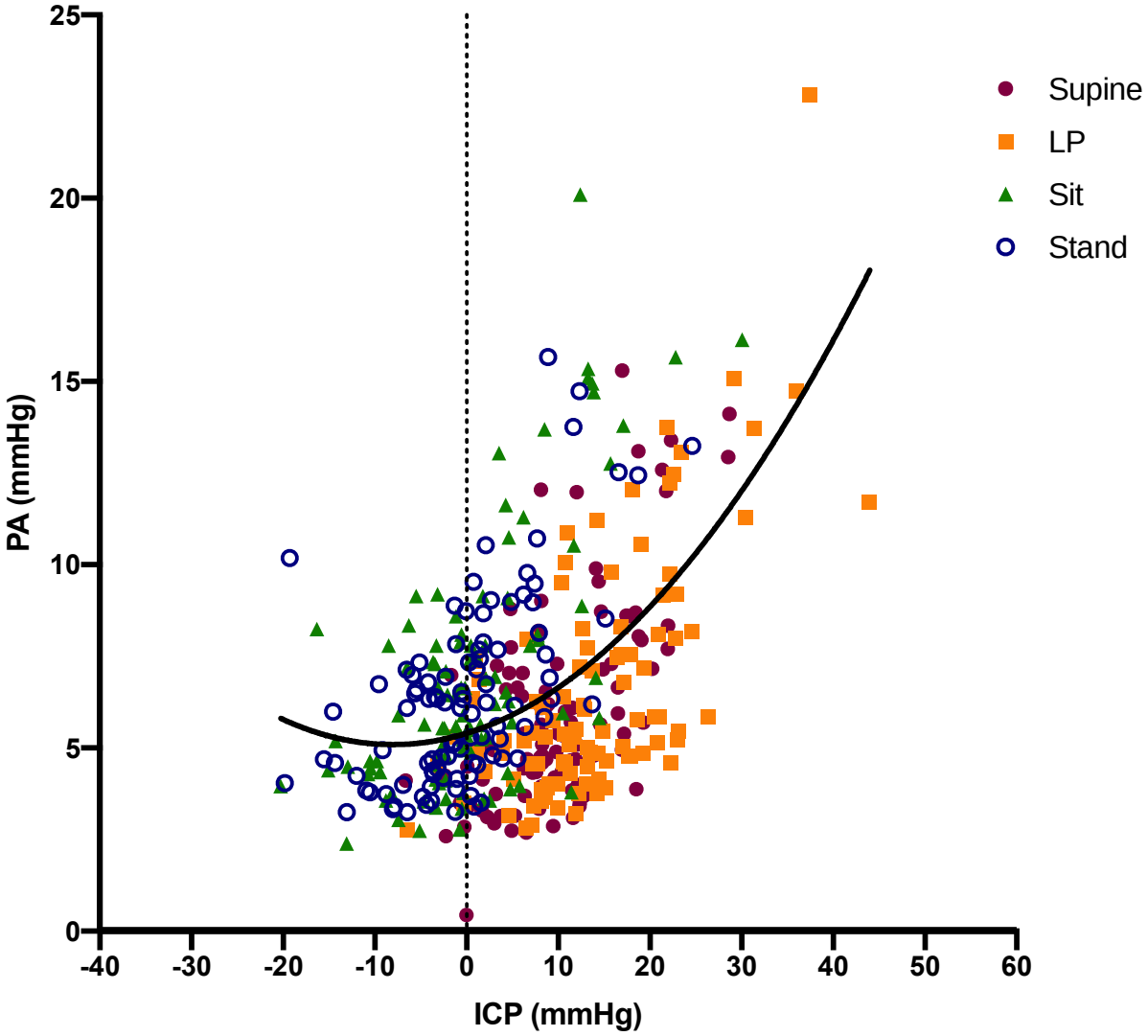
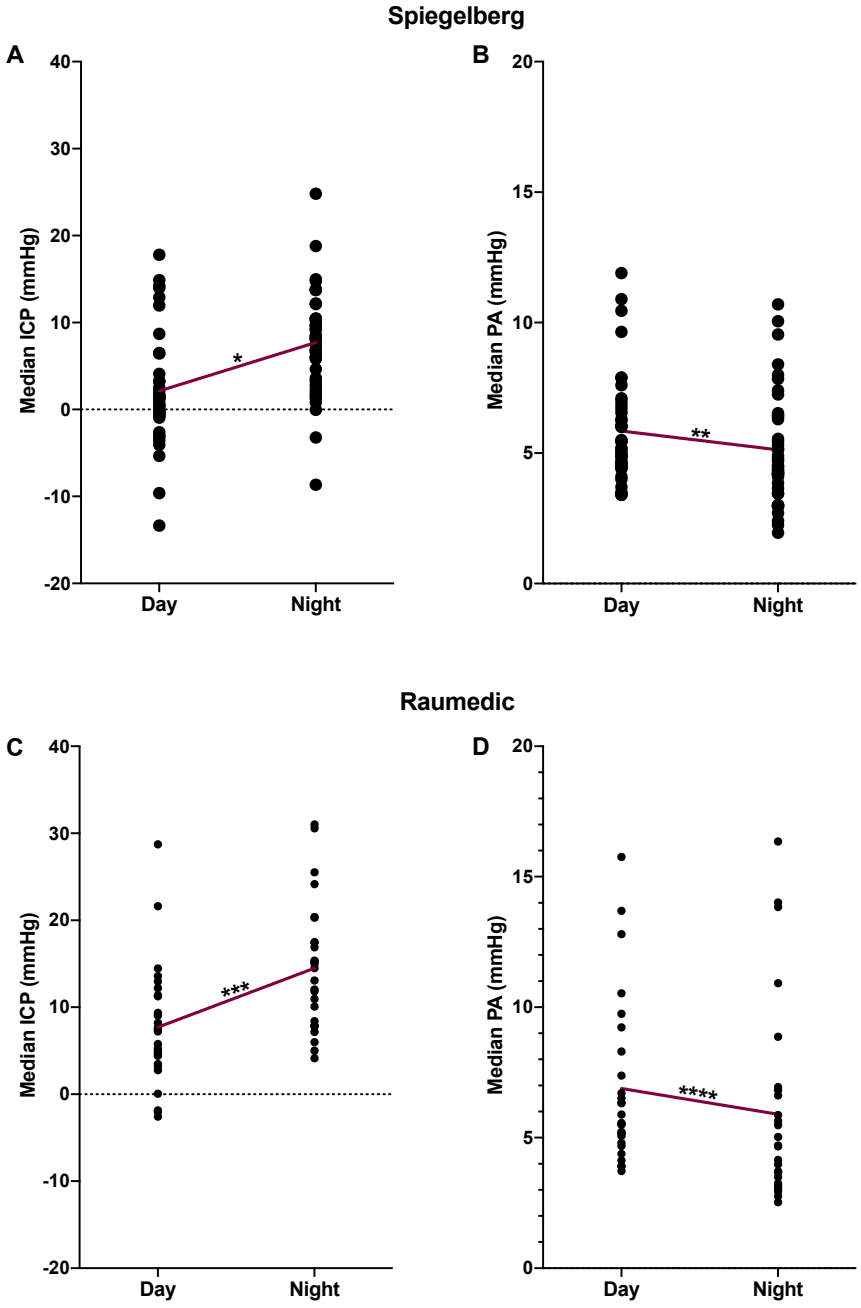


Figure 4. Scatter plot of median day/night intracranial pressure (ICP) and pulse amplitude (PA) for Spiegelberg (A-B) and Raumedic sensors (C-D). Line of best fit and results of significant adjusted linear regression models are displayed. Only patient without shunts are included.



* β=7, 95% CI 5.1 to 8.8, p< 0.001, adjusted R^2=0.64;
** β=-2.1, 95% CI -2.9 to -1.4, p<0.001, adjusted R^2=0.50;
*** β=8.3, 95% CI 6.2 to 10.5, p<0.001, adjusted R^2=0.75;
**** β=-3.9, 95% CI -5.1 to -2.6, p<0.001, adjusted R^2=0.65