Postural influence on intracranial and cerebral perfusion pressure in ambulatory neurosurgical patients

L.G. Petersen¹, J.C.G. Petersen¹, M. Andresen², N.H. Secher³, and M. Juhler²

¹Department of Biomedical Sciences, Faculty of Health Sciences, University of Copenhagen
²Departments of Neurosurgery and ³Anesthesia, The Copenhagen Muscle Research Centre, Rigshospitalet, University of Copenhagen, Denmark

Corresponding author: Lonnie G. Petersen, Department of Biomedical Sciences, Faculty of Health Sciences, The Panum Institute, University of Copenhagen, Blegdamsvej 3, DK-2200 Copenhagen N, Denmark. Fax: (+45) 3532 7418. Telephone: (+45) 2993 4902. E-mail: lonnie@sund.ku.dk.

Running head: Posture and ICP

Key words: Gravity; Hydrostatic pressure; Posture
Abstract

We evaluated postural effects on intracranial pressure (ICP) and cerebral perfusion pressure (CPP: mean arterial pressure (MAP) – ICP) in neurosurgical patients undergoing 24-hour ICP monitoring as part of their diagnostic workup. We identified 9 patients (5 women, age 44±20 yrs.; mean±SD) who were “as normal as possible” i.e. without indication for neurosurgical intervention (e.g. focal lesions, global edema, abnormalities in ICP-profile or cerebrospinal fluid dynamics). ICP (tip-transducer probe, Raumedic) in the brain parenchyma (N=7) or in the lateral ventricles (N=2) and cardiovascular variables (Nexfin) were determined from 20° head-down tilt to standing up. Compared to the supine position, ICP increased during 10° and 20° of head-down tilt (from 9.4±3.8 to 14.3±4.7 and 19±4.7 mmHg, P<0.001). Conversely, 10° and 20° head-up tilt reduced ICP to 4.8±3.6 and 1.3±3.6 mmHg and ICP reached -2.4±4.2 mmHg when standing up (P<0.05). Concordant changes in MAP maintained CPP at 77±7 mmHg regardless of body position (P=0.95). During head-down tilt, the increase in ICP corresponded to a hydrostatic pressure gradient with reference just below the heart, likely reflecting the venous hydrostatic indifference point. When upright, the decrease in ICP was attenuated, corresponding to formation of a separate hydrostatic gradient with reference to the base of the skull, likely reflecting the site of venous collapse. ICP therefore seems to be governed by pressure in the draining veins and collapse of neck veins may protect the brain from being exposed to a large negative pressure when upright. Despite positional changes in ICP, MAP keeps CPP tightly regulated.
**Introduction**

Body position affects blood and fluid distribution and thus regional pressures (7, 17, 31), but there are only few reports on postural influence on intracranial pressure (ICP; 3, 10). Most reports are based on extrapolated values of cerebrospinal fluid (CSF) pressure measured at the lumbar level, with pressure estimated to be zero at the base of the brain when upright (11, 14, 24) and therefore assumed to be negative within the brain (32). ICP depends on the volume of cerebral blood and CSF for which the vascular component is influenced by systemic blood pressure, modified by cerebral autoregulation and venous outflow resistance (12) while the CSF component is described by Davson’s equation (13) as a balance between CSF formation, CSF outflow resistance and venous pressure in the sagittal sinus. It therefore seems that, given intact cerebral autoregulation and systemic blood pressure regulation, positional changes in ICP are dominated by venous pressure. At head-up tilt angles above 10-30° neck-veins start to collapse and internal jugular venous pressure approaches zero (14, 18). On the other hand, if the veins of the neck stay open when upright, a marked negative pressure could develop and thus, venous collapse at the level of the neck may serve to protect the brain from being exposed to large negative pressures (30). Conversely, in a supine or head-down tilt position as well as in the absence of gravitational stress, neck-veins remain open (4) allowing the venous pressure to be transmitted to the brain.

ICP is important for estimating cerebral perfusion pressure (CPP = mean arterial pressure (MAP) - ICP; 26). Sufficient CPP is required to maintain adequate cerebral blood flow (11, 34) and in the case of intracranial disease or head-trauma, treatment is often directed towards maintaining CPP. However, no consensus has been reached regarding target-values (28, 33, 36) and normal range, while also possible effects of posture on CPP have yet to be determined (8).

For ethical reasons, it is not possible to measure ICP invasively in healthy humans. It remains debated whether lumbar CSF pressure reflects ICP accurately especially during changes in
posture (15, 40). As non-invasive estimates of ICP are not currently reliable enough to replace invasive measurements (21), we determined postural effects on ICP in selected ambulatory neurosurgical patients with a tip-transducer catheter inserted in the brain parenchyma or within the ventricular system (3). ICP and central cardiovascular variables were measured from a 20° head-down tilted position to upright standing to test the hypotheses that short-term positional changes in ICP depend on pressure in the draining veins while concordant changes in systemic blood pressure maintains CPP regardless of body position.

Methods

The protocol was approved by the Ethical Committee of Copenhagen (H-3-2012-110) and all patients provided oral and written informed consent in compliance with the declaration of Helsinki. From the 98 patients who underwent ambulatory 24 to 48-hour diagnostic parenchymal or ventricular ICP monitoring from November 2013 to November 2014, we identified nine patients who fulfilled the inclusion criteria (Table 1): five females; age 44 (21-70) years (mean and range); height 169 (152-185) cm; weight 69 (52-89) kg; BMI 23.7 (21-26). The included patients were, at the end of the diagnostic workup considered not to be surgical candidates, i.e. they were free of focal lesions or global edema on CT and/or MRI-scan; had a 24-hour ICP-profile within the generally accepted normal range (1) and for the subgroup of patients provided with a ventricular catheter an infusion-test demonstrated normal cerebrospinal fluid dynamics (22). The indications for ICP monitoring included arrested congenital hydrocephalus (N=4); unexplained headache/fatigue and assessment for possible idiopathic intracranial hypertension (N=3); and headache/fatigue following trauma (one with a head/neck trauma nine years earlier; one with a subdural hematoma 6 years earlier).
**Instrumentation**

All ICP measurements were performed using a tip-transducer catheter (Neurovent-P, Raumedic GmBH, Germany) inserted under local anaesthesia and sterile conditions through a right frontal burr hole. In 7 patients the tip of the probe was inserted 2 cm into the brain parenchyma and in 2 patients the tip of the probe was placed in the frontal horn of the right lateral ventricle at a depth of 5-6 cm. Using pulse wave analysis, cardiovascular variables (blood pressure, heart rate, stroke volume, cardiac output, and total peripheral resistance) were determined by the volume-clamp method from a cuff around the third finger of the non-dominant hand (COtrek, Nexfin, BMeye, The Netherlands) and referenced to the 4th intercostal space using a height sensor. Analog data were transferred to a computer via an analog-to-digital (AD) converter (Powerlab; ADInstruments, NSW, Australia) at 1000 Hz.

**Protocol**

Cardiovascular variables and ICP are presented as the average of the last minute following a 5 min rest period in each of six positions in a randomised order: standing, supine, and during 10° and 20° head-up and head-down tilt.

**Statistics**

A one-way ANOVA (SAS Enterprise guide 4.3, SAS Institute, Cary, NC) for repeated measures and post hoc multiple-range test (Tukey-Kramer) was used to detect statistically significant differences (P < 0.05) compared to the supine position with data presented as mean (SD).

**Results**
Compared to the supine position head-up or down tilt to 10° and 20° did not change central cardiovascular variables significantly. Standing up increased MAP from 87±8 to 103±19 mmHg (P < 0.05) and reduced stroke volume from 107±22 to 92±44 ml (P = 0.002), while heart rate increased from 62±9 to 75±11 bpm thus maintaining cardiac output (P = 0.89) and increasing total peripheral resistance increased from 1242±244 to 1623±490 mmHg/l/min (P < 0.0001; Table 2).

In the supine position parenchymal ICP (N=7) was 8.9±3.7 mmHg and increased with both 10° and 20° head-down tilt to 14.6±4.7 mmHg, P=0.008 and 20±4.7 mmHg, P < 0.0001, respectively. Conversely, head-up tilt to 10° and 20° decreased parenchymal ICP to 5.1±3.7 mmHg, (P = 0.0003) and -0.2±4 mmHg (P < 0.001) respectively, and ICP reached -5.4±5 mmHg when standing up (P < 0.0001).

Ventricular ICP (N=2) in the frontal horn of the right lateral ventricle was 11 and 12 mmHg when supine and increased with 10° (to 16 and 22 mmHg) and 20° head-down tilt to 19 and 23 mmHg. Conversely, head-up tilt to 10° and 20° decreased ventricular ICP to 7 and 8 mmHg and 2 and 5 mmHg, respectively. In the upright position ventricular ICP was -2 and 2 mmHg (Table 2).

**Correlations and the hydrostatic pressure gradient**

In the absence of obstructive lesions CSF circulates freely within the skull, and it can be assumed that ICP is uniformly distributed within the skull (36). Pressures obtained from the parenchyma or the ventricle (i.e. 3 cm more caudal in the brain) can therefore be assumed congruent and combined when corrected for the hydrostatic pressure gradient. The level of the ventricles was chosen to reflect mid-brain level (ICP_{Midbrain}). Parenchymal pressures were therefore corrected by adding the hydrostatic pressure difference during head-up tilt and subtracting the gradient during head-down tilt. MAP was likewise corrected from the 4th intercostal space to reflect mid-brain level (Table 2) and CPP calculated as $CPP = MAP_{Midbrain} - ICP_{Midbrain}$. 
ICP\textsubscript{Midbrain} (N=9) was 9.4±3.8 mmHg in the supine position and increased with both 10\(^{\circ}\) and 20\(^{\circ}\) of head-down tilt to 14.3±4.7 (P = 0.007) and 19±4.7 mmHg (P<0.0001), respectively. Conversely, 10\(^{\circ}\) and 20\(^{\circ}\) head-up tilt reduced ICP\textsubscript{Midbrain} to 4.8±3.6 (P = 0.007) and 1.3±3.6 mmHg and when standing up, ICP\textsubscript{Midbrain} reached -2.4±4.2 mmHg (P < 0.001). Concordant changes in MAP maintained CPP at midbrain-level regardless of position at 77.1±5 mmHg; range: 75 – 79 (P = 0.95, Fig. 1 and 2).

From the change in ICP\textsubscript{Midbrain} at a given tilt-angle (\(\alpha\)), the height of the corresponding hydrostatic fluid column was calculated as \(\text{ICP}(\alpha) - \text{ICP}(0) = \sin(\alpha) \times \text{hydrostatic column} \times \text{density of the fluid}\). During head-down tilt; the observed ICP\textsubscript{Midbrain} increased corresponding to a hydrostatic fluid pressure from a column of approximately 35 cm and thus with reference just below the heart, which was consistent during head-up tilt to 10\(^{\circ}\). At 20\(^{\circ}\) head-up tilt the decrease in ICP was slightly attenuated, and corresponded to a hydrostatic gradient of approximately 30 cm. When standing upright, the decrease in ICP\textsubscript{Midbrain} correlated to a hydrostatic pressure column of only 12-15 cm and thus with reference to the base of the skull (Fig. 2).

**Discussion**

These results suggest that short-term postural changes in ICP are dominated by cephalic venous pressure as predicted by the height of the assumed hydrostatic gradient. During head-down tilt the increase in ICP was greater than the decrease caused by head-up tilt suggesting formation of a smaller hydrostatic gradient possibly caused by collapse of major neck veins. Regulation of systemic blood pressure maintained CPP regardless of body position (Fig. 1).

In upright postures, gravity displaces blood and fluid to dependant regions so that pressures increase towards the feet thus forming hydrostatic pressure gradients though all fluid filled compartments of the body (41). When lying down venous pressure increases towards the head
and accordingly there is a point or level, where pressure remains independent of posture, referred to as the venous hydrostatic indifference point ($\text{HIP}_{\text{vein}}$; 17). We have determined $\text{HIP}_{\text{vein}}$ to be located 7 cm below the 4th inter-costal space (31). A hydrostatic indifference point, or HIP, exists within all fluid filled compartments and reflects the balance between the hydrostatic pressure and mechanical properties of the compartment walls. For the arterial system, $\text{HIP}_{\text{arterial}}$ has been estimated at the level of the aortic arch (17), while for the CSF system, a $\text{HIP}_{\text{CSF}}$ has been estimated somewhere between C6 and Th5 (24).

During head-down tilt, $\text{ICP}_{\text{Midbrain}}$ increased corresponding to a hydrostatic fluid pressure from a column of some 35 cm, i.e. with a reference just below the heart and corresponding to the location of the $\text{HIP}_{\text{vein}}$ (31). It therefore seems that, given an open venous system, the pressure is transmitted to the brain. Conversely the decrease in ICP during head-up tilt head-up tilt angles above 20° was attenuated and when upright, $\text{ICP}_{\text{Midbrain}}$ correlated to a fluid column of only 12-15 cm, likely reflecting the site of internal jugular venous collapse (14, 18; Fig. 2) and corresponding to where CSF pressure is considered to be zero (14). Had the veins remained open, ICP would have been expected to reach more negative values ($\text{ICP}_{\text{expected}}$, fig1). In the supine position the internal jugular veins constitute the primary route of drainage from the brain, but in upright postures these veins respond to the decreasing transmural pressure and collapse thus acting as Starling resistors (20). Cerebral drainage thereby depends increasingly on alternative pathways such as the vertebral venous system (18, 39, 43), which is believed to remain open and thus could constitute a continuous hydrostatic fluid column and support rather large negative pressures (2, 5). Furthermore, when standing up, CSF is displaced from the skull to the spinal compartment (25). While both displacement of CSF and pressure of alternative venous systems is likely to play a role for ICP, we consider from the present data that overall positional ICP is governed predominantly by pressure in the venous sinus which is in turn influenced by pressure in the internal jugular veins. Collapse of
neck-veins in upright postures, i.e. the internal jugular veins, therefore seems to counteract development of large negative pressures within the brain (Fig.1).

Our results are in consistence with Davson’s equation stating that given unaltered CSF formation, ICP in all body positions is determined by the sum of CSF outflow resistance and venous pressure in the sagittal sinus, both of which are influenced by hydrostatic forces. Qvarlander et al. (2013) estimated ICP at mid-brain level from CSF lumbar-pressure measurements at 6 angles of head-up tilt and found that the gravitational decrease in estimated ICP correlated to the hydrostatic pressure gradient in the venous system if collapse of the neck veins at higher angels of head-up tilt was assumed (32).

Slight head-down tilt bed-rest is used to simulate the head-ward fluid shift in microgravity and such studies have indicated an initial increase in ICP. Murthy et al. (1992) used a tympanic membrane displacement technique while Macias et al. (2015) used intra-ocular pressure and the cranial ultrasound pulse amplitude and both found increased ICP although no numeric value could be derived (23, 27, 38). Our study using direct measurement of ICP supports these findings of a close relationship between gravitational blood-volume redistribution and ICP as predicted by the hydrostatic gradient to HIP\textsubscript{vein}. A head-ward fluid shift and accompanying increase in ICP is believed to play a role in the headache and nausea experienced by most astronauts during the initial hours or days in weightlessness (37). These symptoms appear to resolve after hours or days, which is consistent with head-down tilt weightlessness-simulation studies, indicating attenuation of the increase in ICP (35). Adaptive mechanisms to weightlessness include a reduction in blood and total fluid volume (19), altered cerebral autoregulation (6), and changes in compliance of vasculature, membranes and bony structures (29, 42). Gabrion et al. (1995) found that a head-ward fluid shift induced by either weightlessness (9 and 14 days during NASA STS 40 and 56 missions) or (9 or 14 days) tail-suspension of rats, caused similar changes in the choroidal plexus, indicating reduced
CSF formation, which could attenuate ICP during long term head-down tilt or weightlessness (16, 35). Shortly after return to earth or termination of tail-suspension (within 8 hours), the rats displayed return towards normal choroidal differentiation (16). ICP thus seems to adapt to weightlessness.

As neck-veins remain open for the duration of a stay in space (4), venous pressure is continuously transmitted to the brain, unlike on earth where veins collapse when standing up thus creating a separate hydrostatic pressure system separating cerebral pressures from systemic venous pressure. Central venous pressure has been shown to decrease in space compared to supine and head-down positions (9), and an increase in ICP during weightlessness above supine levels is therefore speculative. However, the lack of orthostatic collapse of neck-veins in space, and thus lack of positional “unloading” of ICP may be one of the mechanisms responsible for remodelling of the eye and changes in vision experienced by some astronauts during long-term space mission, changes which are usually seen in association with persistently increased ICP.

Pressure regulation within the brain differs from that of other fluid filled compartments in the body as the brain is enclosed in a rigid skull in which the sinus and large veins are suspended, and can therefore support a negative pressure. On the other hand, the steep pressure/volume relationship implies that even a moderate increase in volume will increase pressure and possibly impede cerebral blood flow (11). A sufficient perfusion gradient across the brain is pivotal for maintaining cerebral blood flow. In the intensive neurosurgical ward, treatment is directed towards maintaining CPP, however, target values and normal range of CPP are unknown and thus CPP-guided therapy remains controversial (8). This study indicates that CPP is tightly regulated within a range of some 75-80 mmHg despite positional variation in ICP.

Limitations
The patients were selected to be “as normal as possible”; i.e. not diagnosed with a neurosurgical disorder at the end of their diagnostic work-up. However, it remains that all had an indication for undergoing ICP-monitoring, and it cannot be ruled out that these patients responded differently to gravitational stress than healthy subjects. We consider it to be a strength that the study included patients with different indications for undergoing ICP monitoring, thus reducing the risk of systematic error.

The experiment was carried out at least 12 hours after insertion of the ICP-transducer, however, it is possible that the intervention in itself somehow influenced the biological system we investigated. ICP was measured at two sites; intraparanchymal and 3-4 cm more caudally in the frontal horn of the right lateral ventricle. The patients were selected based on the absence of major pathology and other exclusion criteria rather than probe placement. Uniformly distributed ICP was assumed as space occupying and obstructing lesions were ruled out and all measurements combined.

We did not confirm collapse of neck veins during head-up tilt, however, this has been done previously both visually (ultrasound) and by pressure measurement of the internal jugular vein (14). Although perfusion pressure (CPP) to the brain is maintained during a change in position, we did not measure cerebral blood flow and future research should focus on this.

**Perspectives and Significance**

Pressure in the draining veins seems to be the major contributor to short-term postural changes in ICP, while regulation of systemic arterial blood pressure compensates to maintain CPP regardless of body position; During head-down tilt postural changes in ICP seems to be governed by pressure of the draining veins as predicted by the height of the hydrostatic gradient to the HIP<sub>vein</sub>. During head-up tilt the decrease in ICP was attenuated corresponding to formation of a separate hydrostatic
gradient with reference to the base of the skull, which could be explained by progressive collapse of neck-veins. Collapse of neck-vein thus separate ICP from systemic venous pressures and may in this way protect against development of a large negative pressure within the brain in upright postures. The open venous system in weightlessness allows for continuous transmission of central venous pressure to the brain, and this lack of positional “unloading” of ICP may contribute to the symptoms associated with increased ICP experienced in space.

Acknowledgements
We thank DHB Christoffersen, neurosurgical nurse for help in identifying and including the patients. The study was supported by grants from the Aase and Einer Danielsen’s Foundation.

Disclosures
No conflicts of interest, financial or otherwise, are declared by the author(s).

Author contributions
LGP, NHS and MJ contributed to concept and design of the study. LGP, JCGP and MA performed the experiment. LGP and JCGP analyzed data. LGP, NHS and MA interpreted the results. LGP and MA drafted the paper and prepared figures. LGP, JCGP, MA, NHS and MJ edited, revised and approved manuscript.
References


5. Badeer HS. Does gravitational pressure of blood hinder flow to the brain of the giraffe? *Comp Biochem Physiol* 83:207-211, 1986


35. Steinbach GC, Macias BR, Tanaka K, Yost WT, Hargens AR. Intracranial pressure dynamics assessed by noninvasive ultrasound during 30 days of bed rest. *Aviat Space Environ Med.* 76:85-90, 2005


Fig. 1. Cerebral perfusion pressure (CPP) and intracranial pressure at midbrain level (ICP<sub>Midbrain</sub>). CPP = MAP<sub>Midbrain</sub> - ICP<sub>Midbrain</sub> (mean±SD), plotted along with measured ICP<sub>Midbrain</sub> and expected ICP (as predicted by the height of the venous hydrostatic gradient from HIP<sub>vein</sub> when veins remain open) as a function of the angle of tilt.

Fig. 2. Hydrostatic pressure gradient according to intracranial pressure (ICP) at different angles of tilt. During head-up tilt ICP corresponded to a hydrostatic gradient with reference at the base of the skull, likely reflecting the site of venous collapse, while during head-down tilt the increase in ICP corresponded to a hydrostatic pressure gradient with reference to just below the heart, likely reflecting the venous hydrostatic indifference point.
Fig. 1
Fig. 2.
Table 1. Neurosurgical patients undergoing invasive 24 or 48-hour intracranial pressure monitoring.

<table>
<thead>
<tr>
<th><strong>Inclusion Criteria</strong></th>
<th><strong>Exclusion Criteria</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;18 and &lt;70 years</td>
<td>Supine ICP &lt;0 or &gt;18 mmHg</td>
</tr>
<tr>
<td>Ambulatory 24/48-hour invasive ICP monitoring</td>
<td>Pathological 24-hour ICP profile</td>
</tr>
<tr>
<td>Glasgow Coma Scale 15, normal congenital function and mentally fit to cooperate in the investigation</td>
<td>Shunt treatment</td>
</tr>
<tr>
<td>No history of cardiovascular disease, chronic illness or disability</td>
<td>CT/MRI indications of global edema or focal lesions</td>
</tr>
<tr>
<td>At the end of all diagnostic workup found not to be candidate for surgical intervention</td>
<td>Resistance to outflow ($R_{out}$) &lt; 14 mmHg/ml/min, or otherwise abnormal CSF dynamics assessed by intrathecal infusion-test</td>
</tr>
<tr>
<td></td>
<td>Headache, nausea or other symptoms during tilting</td>
</tr>
</tbody>
</table>
Table 2. Cardiovascular variables, intracranial pressure (ICP) and cerebral perfusion pressure (CPP) in response to 10° and 20° head-up and head-down tilt and standing (90°).

Values are average for one minute following a 5 min rest period in the given body position (mean±SD) HR: heart rate; SV: stroke volume; CO: cardiac output; TPR, total peripheral resistance; MAP: mean arterial pressure; MAP\textsubscript{Midbrain}: mean arterial pressure at the level of the ventricles; ICP\textsubscript{parenchym}: intracranial pressure at the level of the prarenchyma; ICP\textsubscript{Ventric}: intracranial pressure at the level of the frontal horn of the ventricle; ICP\textsubscript{Midbrain}: intracranial pressure at the level of the ventricles; CPP: cerebral perfusion pressure

*P < 0.05 / **P < 0.0001 compared to the supine position.

<table>
<thead>
<tr>
<th>Tilt angle</th>
<th>HR (bpm)</th>
<th>SV (ml)</th>
<th>CO (l/min)</th>
<th>MAP (mmHg)</th>
<th>MAP\textsubscript{Midbrain} (mmHg/l min)</th>
<th>TPR (mmHg (N=7))</th>
<th>ICP\textsubscript{Parenchym} (mmHg (N=2))</th>
<th>ICP\textsubscript{Ventric} (mmHg)</th>
<th>ICP\textsubscript{Midbrain} (mmHg)</th>
<th>CPP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-20°</td>
<td>60±5</td>
<td>106±12</td>
<td>6.8±1.2</td>
<td>88±8</td>
<td>98±8</td>
<td>1255±249</td>
<td>20±4.7</td>
<td>21±4</td>
<td>**19.0±4.7</td>
<td>79±10</td>
</tr>
<tr>
<td>-10°</td>
<td>62±9</td>
<td>112±25</td>
<td>7.4±2.7</td>
<td>86±11</td>
<td>92±11</td>
<td>1192±241</td>
<td>14.6±4.7</td>
<td>19.3±1</td>
<td>*14.3±4.7</td>
<td>75±13</td>
</tr>
<tr>
<td>0°</td>
<td>62±9</td>
<td>107±22</td>
<td>7.0±2.2</td>
<td>87±8</td>
<td>87±8</td>
<td>1242±244</td>
<td>8.9±3.7</td>
<td>11.6±0.5</td>
<td>9.4±3.8</td>
<td>78±10</td>
</tr>
<tr>
<td>10°</td>
<td>61±8</td>
<td>109±25</td>
<td>7.0±2.4</td>
<td>88±9</td>
<td>82±9</td>
<td>1297±235</td>
<td>5.1±3.7</td>
<td>7.4±2.1</td>
<td>*4.8±3.6</td>
<td>77±10</td>
</tr>
<tr>
<td>20°</td>
<td>63±9</td>
<td>107±27</td>
<td>7.1±2.7</td>
<td>88±7</td>
<td>77±7</td>
<td>1302±194</td>
<td>-0.2±4</td>
<td>3.5±1.5</td>
<td>**1.3±3.6</td>
<td>76±9</td>
</tr>
<tr>
<td>90°</td>
<td>**75±11</td>
<td>*92±44</td>
<td>7.1±4.0</td>
<td>*103±19</td>
<td>71±19</td>
<td>**1623±490</td>
<td>-5.4±5</td>
<td>0.1±2.1</td>
<td>**-2.4±4.2</td>
<td>77±12</td>
</tr>
</tbody>
</table>
Table 1. Neurosurgical patients undergoing invasive 24 or 48-hour intracranial pressure monitoring.

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;18 and &lt;70 years</td>
<td>Supine ICP &lt;0 or &gt;18 mmHg</td>
</tr>
<tr>
<td>Ambulatory 24/48-hour invasive ICP monitoring</td>
<td>Pathological 24-hour ICP profile</td>
</tr>
<tr>
<td>Glasgow Coma Scale 15, normal congenital function and mentally fit to cooperate in the investigation</td>
<td>Shunt treatment</td>
</tr>
<tr>
<td>No history of cardiovascular disease, chronic illness or disability</td>
<td>CT/MRI indications of global oedema or focal lesions</td>
</tr>
<tr>
<td>At the end of all diagnostic workup found not to be candidate for surgical intervention</td>
<td>Resistance to outflow ($R_{out}$) &lt; 14 mmHg/ml/min, or otherwise abnormal CSF dynamics assessed by intrathecal infusion-test</td>
</tr>
<tr>
<td></td>
<td>Headache, nausea or other symptoms during tilting</td>
</tr>
</tbody>
</table>
Table 2. Cardiovascular variables, intracranial pressure (ICP) and cerebral perfusion pressure (CPP) in response to 10° and 20° head-up and head-down tilt and standing (90°).

Values are average for one minute following a 5 min rest period in the given body position (mean±SD) HR: heart rate; SV: stroke volume; CO: cardiac output; TPR, total peripheral resistance; MAP: mean arterial pressure; MAP\textsubscript{Midbrain}: mean arterial pressure at the level of the ventricles; ICP\textsubscript{parenchym}: intracranial pressure at the level of the prarenchyma; ICP\textsubscript{Ventric}: intracranial pressure at the level of the frontal horn of the ventricle; ICP\textsubscript{Midbrain}: intracranial pressure at the level of the ventricles; CPP: cerebral perfusion pressure

*P < 0.05 / **P < 0.0001 compared to the supine position.

<table>
<thead>
<tr>
<th>Tilt angle</th>
<th>HR</th>
<th>SV</th>
<th>CO</th>
<th>MAP</th>
<th>MAP\textsubscript{Midbrain}</th>
<th>TPR</th>
<th>ICP\textsubscript{Parenchym}</th>
<th>ICP\textsubscript{Ventric}</th>
<th>ICP\textsubscript{Midbrain}</th>
<th>CPP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-20°</td>
<td>60±5</td>
<td>106±12</td>
<td>6.8±1.2</td>
<td>88±8</td>
<td>98±8</td>
<td>1255±249</td>
<td>20±4.7</td>
<td>21±4</td>
<td>**19.0±4.7</td>
<td>79±10</td>
</tr>
<tr>
<td>-10°</td>
<td>62±9</td>
<td>112±25</td>
<td>7.4±2.7</td>
<td>86±11</td>
<td>92±11</td>
<td>1192±241</td>
<td>14.6±4.7</td>
<td>19.3±1</td>
<td>*14.3±4.7</td>
<td>75±13</td>
</tr>
<tr>
<td>0°</td>
<td>62±9</td>
<td>107±22</td>
<td>7.0±2.2</td>
<td>87±8</td>
<td>87±8</td>
<td>1242±244</td>
<td>8.9±3.7</td>
<td>11.6±0.5</td>
<td>9.4±3.8</td>
<td>78±10</td>
</tr>
<tr>
<td>10°</td>
<td>61±8</td>
<td>109±25</td>
<td>7.0±2.4</td>
<td>88±9</td>
<td>82±9</td>
<td>1297±235</td>
<td>5.1±3.7</td>
<td>7.4±2.1</td>
<td>*4.8±3.6</td>
<td>77±10</td>
</tr>
<tr>
<td>20°</td>
<td>63±9</td>
<td>107±27</td>
<td>7.1±2.7</td>
<td>88±7</td>
<td>77±7</td>
<td>1302±194</td>
<td>-0.2±4</td>
<td>3.5±1.5</td>
<td>**1.3±3.6</td>
<td>76±9</td>
</tr>
<tr>
<td>90°</td>
<td>**75±11</td>
<td>*92±44</td>
<td>7.1±4.0</td>
<td>*103±19</td>
<td>71±19</td>
<td>**1623±490</td>
<td>-5.4±5</td>
<td>0.1±2.1</td>
<td>**-2.4±4.2</td>
<td>77±12</td>
</tr>
</tbody>
</table>