7. Cerebral perfusion pressure: Definitions. Implication on management protocols. What happens when CPP is too low, and when it is too high? Non-invasive CPP?
The relation between intracranial pressure, mean arterial pressure and cerebral blood flow in patients with severe head injury.

Gobiet W, Grote W, Bock WJ

Abstract
In patients with severe head injuries ICP, MAP and CBF were measured continuously. In most patients there was a positive vasopressor response to increasing ICP, but the ICP/MAP ratio varied considerably in individual cases. CBF was diminished either by increasing ICP or by decreasing MAP. This effect was more marked with ICP above 40 mm Hg or MAP below 110 mm Hg. In terminal stages there was often a negative MAP/ICP ratio accompanied by massive cerebral hyperaemia. Key words: Severe head injury--intracranial pressure--mean arterial pressure--cerebral blood flow--cerebral perfusion pressure--critical limit of ICP and CBF. Abbreviations: ICP equals intracranial pressure (mm Hg); CBF, Flow equals cerebral blood flow (ml/min); MAP equals mean arterial pressure (mm Hg); CPP equals cerebral perfusion pressure (mm Hg) (difference between MAP and ICP); BP equals blood pressure.
PERFUSION PRESSURE (static)

Inflow

\( P_{\text{inflow}} \)

Outflow

\( P_{\text{outflow}} \)

Perfusion pressure = \( P_{\text{inflow}} - P_{\text{outflow}} \)

Inflow

ABP ← Carotid Artery

Outflow

Bridging Veins → ICP

Sagittal sinus

\[ m\text{CPP} = m\text{ABP} - m\text{ICP} \]

Thanks to Dr. E. Schmidt
CPP = meanABP - meanJugularVeinPressure
CPP = meanABP - meanSagittalSinusPressure
CPP = meanABP - mean ICP
CPP = meanABP - mean CriticalClosingPressure
Data from Wakefield, early 1990s
CPP determines brain blood perfusion when ICP is elevated, otherwise ABP is main determinant.
Clinical case: Brain Tissue O2 versus CPP in refractory intracranial hypertension
Cerebral perfusion pressure: management protocol and clinical results

MICHAEL J. ROSNER, M.D., SHEILA D. ROSNER, R.N., M.S.N.,
AND ALICE H. JOHNSON, R.N., B.S.N.

Division of Neurological Surgery, Department of Surgery, University of Alabama at Birmingham,
Birmingham, Alabama

Early results using cerebral perfusion pressure (CPP) management techniques in persons with traumatic brain injury indicate that treatment directed at CPP is superior to traditional techniques focused on intracranial pressure (ICP) management. The authors have continued to refine management techniques directed at CPP maintenance.

One hundred fifty-eight patients with Glasgow Coma Scale (GCS) scores of 7 or lower were managed using vascular volume expansion, cerebrospinal fluid drainage via ventriculostomy, systemic vasopressors (phenylephrine or norepinephrine), and mannitol to maintain a minimum CPP of at least 70 mm Hg. Detailed outcomes and follow-up data bases were maintained. Barbiturates, hyperventilation, and hypothermia were not used.

Cerebral perfusion pressure averaged 83 ± 14 mm Hg; ICP averaged 27 ± 12 mm Hg; and mean systemic arterial blood pressure averaged 109 ± 14 mm Hg. Cerebrospinal fluid drainage averaged 100 ± 98 cc per day. Intake (6040 ± 4150 cc per day) was carefully titrated to output (5460 ± 4000 cc per day); mannitol averaged 188 ± 247 g per day. Approximately 40% of these patients required vasopressor support.

Patients requiring vasopressor support had lower GCS scores than those not requiring vasopressors (4.7 ± 1.3 vs. 5.4 ± 1.2, respectively). Patients with vasopressor support required larger amounts of mannitol, and their admission ICP was 28.7 ± 20.7 versus 17.5 ± 8.6 mm Hg for the nonvasopressor group. Although the death rate in the former group was higher, the outcome quality of the survivors was the same (Glasgow Outcome Scale scores 4.3 ± 0.9 vs. 4.5 ± 0.7). Surgical mass lesion patients had outcomes equal to those of the closed head-injury group.

Mortality ranged from 52% of patients with a GCS score of 3 to 12% of those with a GCS score of 7; overall mortality was 29% across GCS categories. Favorable outcomes ranged from 35% of patients with a GCS score of 3 to 75% of those with a GCS score of 7. Only 2% of the patients in the series remained vegetative and if patients survived, the likelihood of their having a favorable recovery was approximately 80%. These results are significantly better than other reported series across GCS categories in comparisons of death rates, survival versus dead or vegetative, or favorable versus nonfavorable outcome classifications (Mantel–Haenszel χ², p < 0.001). Better management could have improved outcome in as many as 35% to 50% of the deaths.

KEY WORDS • cerebral perfusion pressure • intracranial pressure • traumatic brain injury • therapy
Fig. 4. Scatterplot depicting the relationship between intracranial pressure (ICP) and cerebral perfusion pressure (CPP), which is described by the quadratic equation $ICP = 0.006 \text{CPP}^3 - 1.34 \text{CPP} + 95$ ($p < 0.001$). Note that the lowest ICP for the group will occur at a CPP of approximately 112 mm Hg. There is no tendency for high CPP to potentiate intracranial hypertension.
Decreases in CPP produces gradual decrease in SjvO2

Fig. 7 Effect of changes in CPP produced by increases in ICP (open circles) or decreases in MAP (closed circles) on SjvO₂. Note the reduction in SjvO₂ at CPP values below 60–70 mmHg implying exhaustion of autoregulatory vasodilatation and reliance on increased oxygen extraction to maintain oxygen metabolism. Redrawn from Chan et al.²⁷.

Cerebral protection in severe brain injury: physiological determinants of outcome and their optimisation

David K Menon
Department of Anaesthesia, University of Cambridge Clinical School, Addenbrooke's Hospital, Cambridge, UK

Addenbrooke’s NCCU: ICP/CPP management algorithm

All patients with or at risk of intracranial hypertension must have invasive arterial monitoring, CVP line, ICP monitor and RT SjO₂ catheter at admission to NCCU. Aim to establish TCD and multimodality computer within the first six hours of NCCU stay. Interventions in stage II to be targeted to clinical picture and multimodality monitoring. Check whether the patient is in or may be a candidate for research protocols. Guidelines may be modified at the discretion of the consultant in charge.

Treatment grades III and IV only after approval by NCC Consultant.

- Recent CT - low risk of surgical lesion
- No
- CT
- Surgical lesion? CSF drainage? Role for surgical decompression?
- Yes
- surgery

I
- 10-15° head up, no venous obstruction
- CPP ≥ 70 (CVP 6-10; ± PAC)
- SpO₂ ≥ 97%; PaO₂ ≥ 11 kPa, PaCO₂ ≤ 4.5 kPa
- Temp ≤ 37°C; SjO₂ ≥ 55%; blood sugar 4-7 mmol/l
- Propofol 3-5 mg/kg/hr (midazolam ≥ 0.1 mg/kg/hr from day 2)
- Fentanyl 1-2 µg/kg/hr; atracurium 0.5 mg/kg/hr
- Sucralfate 1g & 6 hrly (Ranitidine 50mg 8 hrly iv if no OGT or aspirate >200ml/6 hrs)
- Phenytoin 15 mg/kg if indicated (fists, depressed & etc)

II
- 20% mannitol 2ml/kg X 3 or till plasma 320 mosm/l
- PAC, volume, vasoactives to increase MAP (CPP 90-100)
- Reduce PaCO₂ to 3.5-4.0 kPa providing SjO₂ stays ≥ 55%
- Temp ≥ 35°C, Daily lipid screen if still on propofol
- EEG: ? fits -> Institute or escalate antiepileptic therapy

III
- CPP < 70; ICP > 25 (Check probe, ? re-CT)
- Temp 33°C (discontinue propofol)

IV
- CPP < 70; ICP > 25 (Check probe, ? re-CT)
- Trial of bolus i.v. anaesthetic (e.g. Propofol 50-200 mg), maintain CPP with fluids and vasoactive agents
- If favorable effect on ICP and CPP start thiopentone
- 250 mg boluses up to 3-5 g + infusion 4-8 mg/kg/hr to achieve and maintain burst suppression
Impact of Intracranial Pressure and Cerebral Perfusion Pressure on Severe Disability and Mortality After Head Injury

Marcello Boldrini, Marek Czerny, Peter Hutchinson, Luzia A. Steiner, Magda Hler, Piotr Sniatkowski, and John D. Pickard

Academic Neurosurgical Unit, Addenbrooke's Hospital, Cambridge, UK; Policlinico San Matteo, University of Pavia, Italy; Department of Anaesthesia, University Hospital Basel, Switzerland

Strict CPP protocol introduced in 1997

ABP [mm Hg]

ICP [mm Hg]

CPP [mm Hg]
The “Lund” therapy

A neurocritical care group from Lund, Sweden, have suggested a different approach to the management of patients with severe TBI.

There are two principal aims of the Lund protocol:

1. The prevention of brain oedema formation by reducing fluid shift from capillaries into brain parenchyma
2. The improvement of the cerebral microcirculation by the avoidance of arterial vasoconstrictors.

Brain oedema regulation is targeted by preservation of colloid osmotic pressure. To achieve this goal, the Lund protocol advocates the use of repeated human albumin infusions (aiming for a normal serum albumin concentration) and blood transfusions (aiming for a normal haemoglobin concentration). The patient is kept euvolaemic to slightly hypovolaemic by diuretic therapy. To reduce the hydrostatic pressure in brain capillaries, mean blood pressure is kept at a “physiological level for the age of the patient”. Drugs employed to achieve this goal are metoprolol and clonidine, and thiopentone and dihydroergotamine in an attempt selectively to cause vasoconstriction of the precapillary vessels (via flow-metabolism coupling). Dihydroergotamine is also prescribed with the purpose of constricting cerebral veins in order to reduce brain volume.

The Lund approach to the management of intracranial hypertension and CPP has fuelled controversy. If the ICP is normal, CPP is maintained at 60-70 mmHg. However, if the ICP is elevated, and the above therapies fail to reduce brain volume, a CPP of 50 mmHg is accepted (40 mmHg for children).

Inotropes such as dobutamine are avoided because of the risk of β2-receptor-mediated, cerebral vasodilatation increasing intracranial blood volume. Vasoconstrictors such as noradrenaline are avoided, as they are feared to cause brain ischaemia secondary to α-receptor-stimulated capillary constriction.

The only published trial using the Lund protocol is a small, non-randomised study (53 patients in the treatment group) with a historical control group. The control group comprised 38 patients treated between 1982 and 1986. Study patients had a huge mortality benefit and favourable neurological outcome at 6 months. A large, randomised, controlled trial is still awaited.

8% mortality after Severe TBI. Is it credible?
Outcome seems to be associated with mean CPP (529 head injuries, Addenbrooke’s Hospital)
The Lower Limit of Cerebral Blood Flow Autoregulation Is Increased with Elevated Intracranial Pressure

Ken M. Brady, MD
Jennifer K. Lee, MD
Kathleen K. Kilibr, BS
Ronald B. Easley, MD
Raymond C. Koehler, PhD
Marek Czsonyka, PhD
Peter Smielewski, PhD
Donald H. Shaffner, MD

BACKGROUND: The cerebral perfusion pressure that denotes the lower limit of cerebral blood flow autoregulation (LLA) is generally considered to be equivalent for reductions in arterial blood pressure (ABP) or increases in intracranial pressure (ICP). However, the effect of decreasing ABP at different levels of ICP has not been well studied. Our objective in the present study was to determine if the LLA during arterial hypotension was invariant with ICP.

METHODS: Using continuous ventricular fluid infusion, anesthetized pigs were assigned to 1 of 3 groups: naïve ICP (n = 10), moderately elevated ICP (20 mm Hg; n = 11), or severely elevated ICP (40 mm Hg; n = 9). Gradual hypotension was induced by inflation of a balloon catheter in the inferior vena cava. The LLA was determined by monitoring cortical laser-Doppler flux.

RESULTS: The naïve ICP group had an average CPP at the LLA (LLA CPP) of 29.8 mm Hg (65% CI: 26.5–33.0 mm Hg). However, the moderately elevated ICP group had a mean LLA CPP of 37.6 mm Hg (65% CI: 32.0–43.2 mm Hg), and the severely elevated ICP group had a mean LLA CPP of 51.4 mm Hg (65% CI: 41.2–61.7 mm Hg). The LLA significantly differed among groups, and the increase in LLA correlated with the increase in ICP.

CONCLUSIONS: In this atraumatic, elevated ICP model in pigs, the LLA had a positive correlation with ICP, which suggests that compensating for an acute increase in ICP with an equal increase in ABP may not be sufficient to prevent cerebral ischemia.

Thanks to Dr. K. Brady

Figure 1. Autoregulation curves for three conditions of intracranial pressure (ICP) in piglets. Laser-Doppler flux measurements are used to construct autoregulation curves in three conditions of ICP in piglets: naïve (n = 10), ICP 20 mm Hg (n = 11), and ICP 40 mm Hg (n = 9). Values are binned in 5-mm Hg increments of CPP. The lower limit of autoregulation (LLA) was determined separately for each animal as the intersection of the two best-fit lines describing the laser-Doppler flux/cerebral perfusion pressure (CPP) scatter plot, and the average LLA for each group is shown as a vertical dashed line (29.8 mm Hg for the naïve group, 37.6 mm Hg for the elevated ICP group and 51.4 mm Hg for the very elevated ICP group).
Thanks to Dr. K. Brady

**Figure 2.** Effect of intracranial pressure (ICP) on the lower limit of autoregulation (LLA). Box-whisker plots showing the LLA for each experimental condition of ICP are shown. The increasing trend in LLA_{CPP} for increasing ICP was significant by Kruskal-Wallis one-way analysis of variance ($P = 0.0018$).

**Figure 3.** Correlation of intracranial pressure (ICP) and cerebral perfusion pressure (CPP) at the lower limit of autoregulation (LLA). A scatter plot of CPP versus ICP at the LLA in all 20 piglets was used to quantify linear correlation ($P < 0.0001$). The slope of the best-fit line is $0.6 \text{ mm Hg CPP/mm Hg ICP}$.
CPP- relationship to pulse amplitude of ICP
CPP too low - ischaemic insult

ABP
mmHg

FV
cm/s
Too high CPP- hyperaemic insult

- ABP (mmHg)
- FV (cm/s)
Non-invasive estimation of CPP

CPP = MAP - ICP

sources of error: ICP & MAP

MAP: where to zero transducer; TCD: how to hold the probe?

Thanks to Pippa Al-Rawi, 2001
CPP can be estimated non-invasively using TCD:

eCPP = \frac{F_1}{F_{Vm}} \times A_1  
(Aaslid, 1986)

Or

nCPP = ABP \times \frac{F_{Vd}}{F_{Vm}} + 14  
(Czosnyka, 1997)
Cerebral perfusion pressure in head-injured patients: a noninvasive assessment using transcranial Doppler ultrasonography


Wolfson Brain Imaging Centre, Medical Research Council/Cambridge Centre for Brain Repair and Academic Neurosurgical Unit, Department of Anaesthesia, and The Neurosciences Critical Care Unit, Addenbrooke’s Hospital, Cambridge, United Kingdom

Object. The authors studied the reliability of a new method for noninvasive assessment of cerebral perfusion pressure (CPP) in head-injured patients in which mean arterial blood pressure (ABP) and transcranial Doppler middle cerebral artery mean and diastolic velocities are measured.

Methods. Cerebral perfusion pressure was estimated (eCPP) over periods of continuous monitoring (20 minutes–2 hours, 421 daily examinations) in 96 head-injured patients (Glasgow Coma Scale score < 13) who were admitted to the intensive care unit. All patients were sedated, paralyzed, and ventilated. The eCPP and the measured cerebral intracranial pressure (measured using an intraparenchymal microsensor) were compared.

The correlation between eCPP and measured CPP was $r = 0.73$, $p < 10^{-4}$. In 71% of the examinations, the error was less than 10 mm Hg and in 84% of the examinations, the error was less than 15 mm Hg. The positive predictive power (94%) for detecting low CPP (< 60 mm Hg). The eCPP also accurately reflected measured CPP over time ($r = 0.8$, $p < 0.001$) in situations such as plateau and B waves of intracranial hypertension, and refractory intracranial hypertension. A good correlation was found between the measured and eCPP when day-by-day variability was assessed in a group of 41 patients ($r = 0.71$).

Conclusions. Noninvasive estimation of CPP by using transcranial Doppler ultrasonography may be useful in which monitoring relative changes in CPP is required without invasive measurement of intracranial pressure.

KEY WORDS • transcranial Doppler ultrasonography • ultrasound • cerebral perfusion • head injury
Good replication of slow trend in direct CPP
Good replication of slow waves in direct CPP
nCPP and direct CPP- offset around 20 mm Hg, but good replication of slow trends
nCPP does not react to changes in direct CPP
Day-by-day evaluation of nCPP after head injury

Thanks to Mr. EA Schmidt
On this particular day ICP transducer was broken. Non-invasive CPP (CPPe) indicated fast decrease. Was it plateau wave of ICP? Raw TCD recordings seem to confirm this interpretation...
Day-by-day evaluation of nCPP. We can find good and bad examples:
Retrospective analysis: 231 head injured patients examined 1995-2003
Prospective study: 25 patients, 105 monitorings:

86% of points within +/- 10 mm Hg limit; 95% limit 12 mm Hg

Both sides nCPP?

Difference between left and right nCPP (dCPP) should give us information on inter-hemispherical gradients of CPP.

Example: monitoring of nCPP during liver transplant
Summary

• CPP is a concept, not a real pressure
• Autoregulation is it only CPP-dependant?
• Too low CPP - ischaemia, too high - hyperaemia
• CPP-oriented protocols: success or failure?
• Non-invasive assessment of CPP important where ICP cannot be monitored directly