19. Monitoring of CA using TCD
Drawing the autoregulatory curve: in clinical practice such dramatic changes in CPP are not permissible
Monitoring cerebral autoregulation -
certainly not a new concept


CEREBRAL AUTOREGULATION

Testing
* Clear stimulation:
  - drug to rise ABP
  - leg cuff release
  - head down tilt
  - lower body pressure
  - slow respiration
  - transient compression

• Better accuracy
• One-off measurement

Monitoring
* No stimulation;
  spontaneous waves of ABP or CPP

• Worse accuracy (SNR worse)
• Information continuous in time – may be time-averaged
Mx is ‘noisy’; it requires time-averaging. However it may explain changes in cerebral autoregulation which happen in time.
Monitoring of transient phenomena: Positive Mx indicates loss of cerebral autoregulation at the top of plateau waves

CONTINUOUS MONITORING OF CA: TIME-RELATED CHANGES
Monitoring of Cerebrovascular Autoregulation: Facts, Myths, and Missing Links

Marek Czosnyka · Ken Brady · Matthias Reinhard · Piotr Snielewski · Luzius A. Steiner
Administration of hypertonic saline - case after SAH
Validation of Mx: Positive correlation with static rate of autoregulation (SROR) in 17 head injured patients

Validation: Transient Hyperaemic Response Test (Short [6-8 sec] compression of the CCA)

**THRT Positive**
Intact Autoregulation

THRR = 1.45

**THRT Negative**
Impaired autoregulation

THRR = 0.95

THRT agrees with Mx in HI (N=47 patients)

Smielewski P, Czosnyka M, Kirkpatrick P, Pickard JD.
Correlation between Mx and CO$_2$-Reactivity in Carotid Disease


Angiography:
Ipsilateral stenosis: 95%
Contralateral stenosis: 70%
Relatively good correlation between phase shift, CO2 reactivity and correlation index in patients with carotid stenosis

Reinhard M, Roth M, Muller T, Czosnyka M, Timmer J, Hetzel A. Cerebral autoregulation in carotid artery occlusive disease assessed from spontaneous blood pressure fluctuations by the correlation coefficient index. Stroke. 2003 Sep;34(9):2138-44
Clinical Article
Pressure-autoregulation, CO₂ reactivity and asymmetry of haemodynamic parameters in patients with carotid artery stenotic disease. A clinical appraisal

I. Gooskens¹, E. A. Schmidt¹, M. Czosnyka¹, St. K. Piechnik¹, P. Smielewski², P. J. Kirkpatrick¹, and J. D. Pickard¹,²

FV=a*EtCO₂+b*ABP

![Graph showing correlation between ABP and Autoregulation Index Mx]

Fig. 1. Example of CO₂ reactivity test. ABPm: mean arterial blood pressure, FVm: mean flow velocity, EtCO₂: end tidal CO₂

![Graph showing relationship between ABP-corrected CO₂ reactivity and Autoregulation Index Mx]

Fig. 3. Relationship between ABP-corrected CR and autoregulation (Mx). Patients with poor reactivity are more likely to have defective pressure autoregulatory responses.
Autoregulation and arterial CO$_2$

Mx responds to PaCO$_2$ during routine CO$_2$-reactivity testing.
Indices of autoregulation should be always CO2-corrected Mx:
0.2 per 1kPa of EtCO2
RoR: -0.13 per 1kPa of EtCO2

Study in volunteers:

Mx well agreed with static rate of autoregulation (leg-cuff test, Aaslid et al, 1983) $R^2=0.66$; N=14, 3 PaCO2 levels

Myth: Patients in different clinical conditions can be compared

1- head injury- survivors
2- head injury- died
3- carotid artery stenosis- unilateral
4- carotid artery stenosis- bilateral
5- volunteers (young)- normocapnia
6- volunteers (young)- hypercapnia
7- SAH patients- no spasm
8- SAH patients- spasm
APPLICATIONS: TBI

Relationship between Mx and CPP replicates Lassen’s curve in head injury - review of 188 cases

HEAD INJURY:
AUTOREGULATION IS SIGNIFICANTLY WORSE IN PATIENTS WITH UNFAVOURABLE OUTCOME

Autoregulation is worse first two days following trauma but only in patients who died (red line)
MxA: calculated with MAP or Mx: calculated with CPP?

Mxa is well correlated with Mx but discrepancies are possible. Generally Mxa > Mx.
Mx correlates with outcome better than Mxa
F statistics values for different autoregulation indices

Many thanks to Mr. K. Budohoski
AUTOREGULATION: SIDE-TO-SIDE DIFFERENCE (60 SEVERELY HEAD INJURED PATIENTS)

Example (rare!) of impaired autoregulation on right side and preserved on left side.

SIDE-TO-SIDE DIFFERENCE IN AUTOREGULATION:

VOLUNTEERS:

HEAD INJURY:

SIDE-TO-SIDE DIFFERENCE IS GREATER IN PATIENTS WITH MIDLINE SHIFT AND IN THOSE WHO DIED:

Mxl – Mxr > 0
i.e. Mxl > Mxr

Worse autoregulation on the Left

Shift from the Left to the Right

Left side expansion

Shift from the Right to the Left

Right side expansion

Worse autoregulation on the Right

Mxl – Mxr < 0
i.e. Mxr > Mxl

Figure 3 a

Figure 3 b
Figure 3 a

Left-right difference in Mx

Midline shift (mm)

r = -0.42
P = 0.03
n = 27
Continuous Assessment of Cerebral Autoregulation in Subarachnoid Hemorrhage

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Cerebral vasospasm remains a leading cause of morbidity and mortality after subarachnoid hemorrhage (SAH). Cerebral ischemia may ensue when autoregulation fails to compensate for spasm. We examined how autoregulation is affected by vasospasm by using transcranial Doppler. The moving correlation coefficient between slow changes of arterial blood pressure and mean or mean flow velocity (FV), termed “Mx” and “Sx,” respectively, was used to characterize cerebral autoregulation. Vasospasm was declared when the mean FV increased to more than 120 cm/s and the Lindgren ratio was more than 3. This occurred in 15 of 32 SAH patients. On the basis of the bilateral transcranial Doppler recordings of the middle cerebral artery in vasospastic patients, Mx and Sx were calculated for baseline and vasospasm. Mx increased during vasospasm (0.46 ± 0.32 mmHg × 1) and was significantly higher (P = 0.02) than at baseline (0.21 ± 0.28). Sx was also increased (0.22 ± 0.2 vs. 0.05 ± 0.2 at baseline, P = 0.05). Mx correlated with mean FV (r = 0.57, P = 0.01) and the Lindgren ratio (r = 0.67, P < 0.01). Mx (P = 0.006) and Sx (P = 0.044) were higher on the vasospastic side (Mx, 0.44 ± 0.27; Sx, 0.28 ± 0.23) than compared with the contralateral side (Mx, 0.34 ± 0.28; Sx, 0.16 ± 0.25). The increased Mx and Sx during cerebral vasospasm demonstrated impaired cerebral autoregulation. Mx and Sx provide additional information on changes in autoregulation in SAH patients.

(Aneasth Analg 2004;98:1133-9)
Subarachnoid haemorrhage

Autoregulation worsens during vasospasm

Unilateral CCA stenosis

Ipsilateral vs contralateral difference in cerebrovascular reactivity are significant and dependant on level of stenosis

Cerebral Autoregulation in Carotid Artery Occlusive Disease Assessed From Spontaneous Blood Pressure Fluctuations by the Correlation Coefficient Index

M. Reinhard, MD; M. Roth, PhD; T. Müller, PhD; M. Czorsyka, PhD; J. Timmer, PhD; A. Hetzel, MD

Background and Purpose—Estimation of dynamic cerebral autoregulation from spontaneous fluctuations of arterial blood pressure (ABP) and cerebral blood flow velocity (CBFV) is an attractive noninvasive option for cerebral hemodynamic impairment. We evaluated the correlation coefficient index method in patients with severe obstructive carotid disease and compared it with transfer function analysis (frequency domain approach to cerebral autoregulation) and CO2 vasomotor reactivity.

Methods—In 139 patients with severe unilateral carotid stenosis (≥70%) or occlusion, CBFV (transcranial Doppler) and ABP (Finapres method) were recorded over 10 minutes. Correlations between systolic pressure, diastolic pressure, and mean ABP and CBFV oscillations over 1-minute epochs were averaged over 10 minutes to form the correlation coefficient indexes (Ds, Dm, Ms, respectively). Transfer function parameters (phase shift and gain between ABP and CBFV oscillations) were determined from the entire 10-minute period. CO2 reactivity was assessed by inhalation of 7% CO2.

Results—The correlation indexes Ds and Ms were significantly higher ipsilateral to stenosis and increased with degree of stenosis, indicating increasing dependence of CBFV on ABP and thus impairment of cerebral autoregulation. Ds and Ms correlated moderately but highly significantly with transfer function parameters and CO2 reactivity and showed a good level of agreement in detecting pathological values. Patients with a small variance of the 1-minute source correlations of Ds and Ms showed clearly better correlation values. Transfer function parameters and CO2 reactivity but not Ds and Ms were significantly poorer in patients with symptomatic stenosis or occlusion.

Conclusions—The potential of the correlation coefficient indexes Ds and Ms in detecting hemodynamic impairment in patients with carotid stenosis is comparable to that of transfer function analysis and CO2 reactivity testing. In future, a combination of various hemodynamic tests might help to identify patients at risk for ischemic events. (Stroke. 2003;34: 2138-2144.)

<table>
<thead>
<tr>
<th>Degree of Stenosis</th>
<th>A, 70–79%</th>
<th>B, 80–89%</th>
<th>C, 90–99%</th>
<th>D, 100%</th>
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<tr>
<td>(N=40)</td>
<td>(n=21)</td>
<td>(n=56)</td>
<td>(n=22)</td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>Unilateral</td>
<td>Unilateral</td>
<td>Unilateral</td>
<td></td>
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</tbody>
</table>

Figure 2. Box plots of autoregulation parameters in different groups of ICA stenosis. ○, Denotes exceeding values (>1.5 box
In patients with normal CSF circulation there is an association with dysautoregulation that is not found in patients with increased resistance to CSF outflow. Does this indicate underlying cerebrovascular disease?

Impaired Autoregulation of Cerebral Blood Flow During Rewarming from Hypothermic Cardiopulmonary Bypass and Its Potential Association with Stroke

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BACKGROUND: Patient rewarming after hypothermic cardiopulmonary bypass (CPB) has been linked to brain injury after cardiac surgery. In this study, we evaluated whether cooling and then rewarming of body temperature during CPB in adult patients is associated with alterations in cerebral blood flow (CBF)–blood pressure autoregulation.

METHODS: One hundred twenty-seven adult patients undergoing CPB during cardiac surgery had transcranial Doppler monitoring of the right and left middle cerebral artery blood flow velocity. Eleven patients undergoing CPB who had arterial inflow maintained at >35°C served as controls. The mean velocity index (Mx) was calculated as a moving linear correlation coefficient between slow waves of middle cerebral artery blood flow velocity and mean arterial blood pressure. Intact CBF–blood pressure autoregulation is associated with an Mx that approaches 0. Impaired autoregulation results in an increasing Mx approaching 1.0. Comparisons of time-averaged Mx values were made between the following periods: before CPB (baseline), during the cooling, and after CPB. The number of patients in each phase of CPB was not an Mx ∼ 0, indicative of impaired CBF autoregulation, was determined.

RESULTS: During cooling, Mx (left, 0.29 ± 0.18; right, 0.28 ± 0.18 [mean ± sd]) was greater than that at baseline (left, 0.17 ± 0.21; right, 0.17 ± 0.20; P ≤ 0.0001). Mx increased during the rewarming phase of CPB (left, 0.40 ± 0.19; right, 0.39 ± 0.19) compared with baseline (P ≤ 0.0001) and the cooling phase (P ≤ 0.0001), indicating impaired CBF autoregulation. After CPB, Mx (left, 0.27 ± 0.20; right, 0.28 ± 0.21) was higher than at baseline (left, P = 0.0004; right, P = 0.0003), no different than during the cooling phase, but lower than during rewarming (left, P ≤ 0.0001; right, P ≤ 0.0005). Forty-three patients (34%) had an Mx ≥ 0.4 during the cooling phase of CPB and 68 (53%) had an average Mx ≥ 0.4 during rewarming. Nine of the 11 warm controls had an average Mx ≥ 0.4 during the entire CPB period. There were 7 strokes and 1 TIA after surgery. All strokes were in patients with Mx ≥ 0.4 during rewarming (P = 0.015). The unadjusted odds ratio for any neurologic event (stroke or transient ischemic attack) for patients with Mx ≥ 0.4 during rewarming was 6.57 (95% confidence interval, 0.79 to 55.0, P < 0.08).

CONCLUSIONS: Hypothermic CPB is associated with abnormal CBF–blood pressure autoregulation that is worsened with rewarming. We found a high rate of strokes in patients with evidence of impaired CBF autoregulation. Whether a pressure-passive CBF state during rewarming is associated with risk for ischemic brain injury requires further investigation.
Figure 8–9  Example of arterial blood pressure (ABP) and transcranial Doppler ultrasonography (TCD) monitoring during liver transplantation. Note worsening of autoregulation (positive mean index [MIx] value) during anhepatic phase, which improves during reperfusion (after 14:30). During reperfusion, noninvasive cerebral perfusion pressure (nCPP) and blood flow velocity (FV) values gradually improve, and critical closing pressure (CCP) decreases (which may indicate either a decrease in intracranial pressure or gradual vasodilation).
A comparison study of cerebral autoregulation assessed with transcranial Doppler and cortical laser Doppler flowmetry

Christian Zweifel, Marek Czosnyka, Andrea Lavinio, Gianluca Castellani, Dong-Joo Kim, Emmanuel Carrera, John D. Pickard, Peter J. Kirkpatrick and Peter Smielewski

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**Neurological Research** 2010

***Mx < LDx. Is cortex more vulnerable than rest of the brain?***
Spontaneous oscillations of CBFV and ABP

Fast Fourier analysis

M-waves: 3 to 9 cpm

B-waves: 0.5 to 3 cpm

coefficients of variance (CoV)

Cross-spectral analysis

coherence (COH ≥ 0.4)

phase angle shift (φ) between –180 and +180°

Thanks to Dr. C. Haubrich
Cross-Spectrum-Analysis between CBFV and ABP

Kohärenzbedingung (COH ≥ 0.4)

Phasenverschiebung M-Wellen (57.5 ± 16.3°)

Diehl, Funktionelle Dopplersonographie in der Neurologie 1996

Thanks to Dr. C. Haubrich
ARI: response of CBF to step change in ABP

Thanks to Prof. R. Panerai
Fig 4. Responses of cerebral autoregulation model to a step change in blood pressure.
Messages to take home:

• CA can be monitored continuously
• Methods: ARI, phase shift, Mx
• Impaired autoregulation predicts bad outcome in TBI
• In vasospasm autoregulation deteriorates
• In unilateral spasm, carotid artery stenotic disease, TBI with midline shift, unilaterally impaired autoregulation indicates haemodynamically relevant asymmetry