

**Ultrasound Assessment
of Cerebral Blood Flow
during Extra-Corporeal Life Support
following Cardiac Arrest**

Background

‘Post-cardiac arrest brain injury’ is the leading cause of death in individuals who achieve stable ROSC following CA. It is common for patients who suffer cardiac arrest and receive ECLS, to die following failure of recovery of neurological function. In the ARREST trial (Yannopoulos et al., Lancet, 2020) 12 patients received V-A ECMO, 6 of whom (50%) had WLST following unsurvivable hypoxic brain injury. In the Prague OHCA trial (Belohlavek et al., JAMA, 2022) 115 of 124 patients randomised to receive V-A ECMO received this therapy, with the majority of non-survivors in this treatment arm dying of either refractory arrest, cardiogenic shock or MOF (58/124, 47%), but with 21 (of 124, 17%) dying of ‘brain death’. In the INCEPTION trial (Suverein et al., NEJM, 2023) 70 patients were randomised to the ECLS treatment arm, cannulation was attempted in 52 (when cannulation was not attempted, this was usually due to the patient developing stable ROSC after randomisation and prior to cannulation), ECMO flow was achieved in 46, of these 39 (of 46, 85%) died within the ICU, in this treatment arm (randomised to ECLS) 56/70 (80%) had WLST, with the most commonly cited reason being ‘neurologically unfavourable’ (24/56, 43%).

The treating team have a number of roles to perform when caring for a patient who is receiving ECLS having suffered a CA, and these include taking measures to maximise the chance of survival with a favourable neurological outcome, and neuroprognostication (determining whether ongoing treatment is likely or unlikely to result in a good outcome). This talk looks at the current literature, to see if there is any evidence that ultrasound assessment of cerebral blood flow (via Trans-Cranial Doppler, TCD) can assist with either of these roles.

NARRATIVE REVIEW

Brain injury after cardiac arrest: pathophysiology, treatment, and prognosis

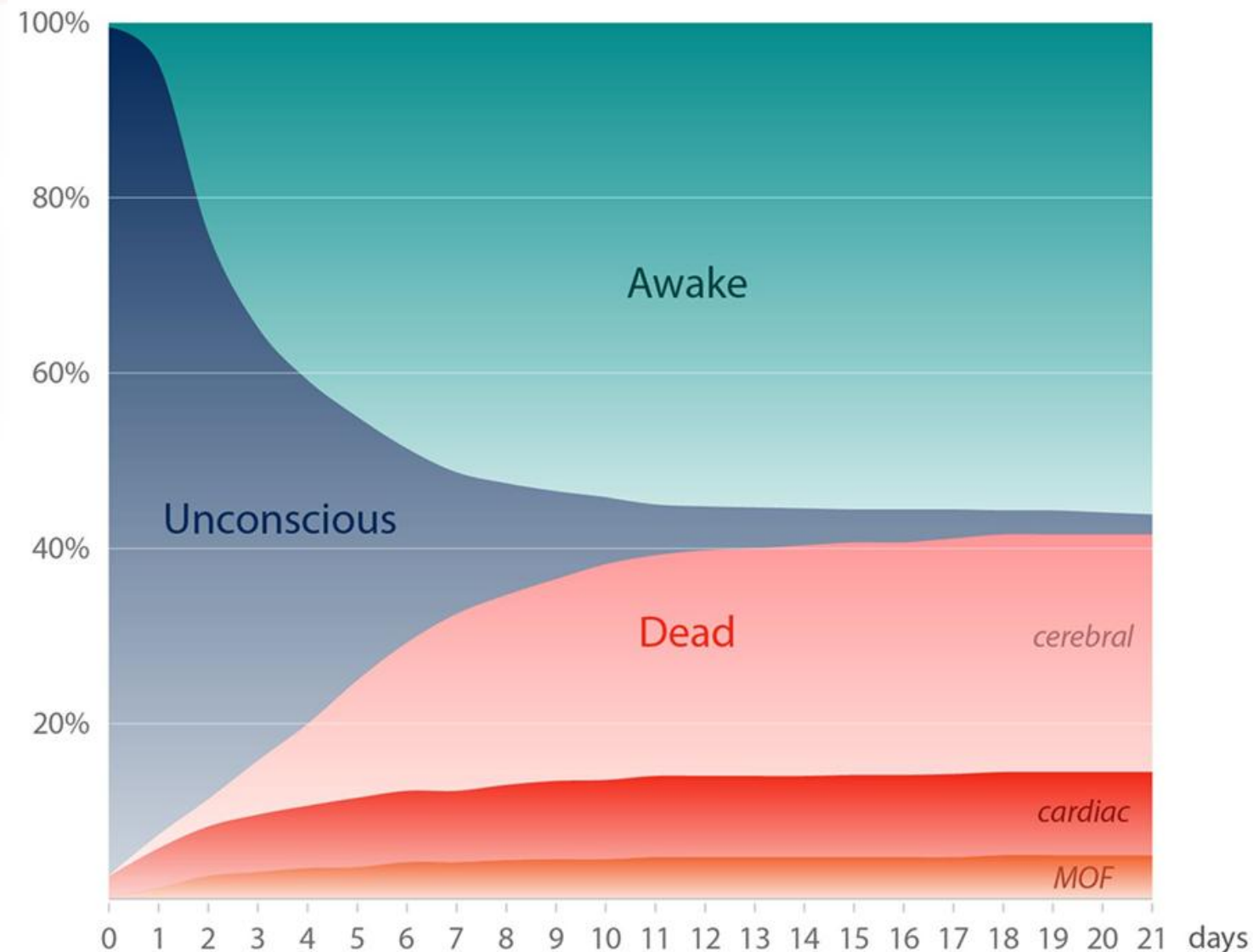
Claudio Sandroni^{1,2*} , Tobias Cronberg³ and Mypinder Sekhon⁴

The Brain after Cardiac Arrest

Jonathan Elmer, MD, MS^{1,2} and Clifton W. Callaway, MD, PhD¹

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Brain injury following cardiac arrest

The brain is exquisitely sensitive to interruption of cerebral blood flow, with consciousness being lost after 4-10s, and an isoelectric EEG developing after just 10-30s of asystole. Cerebral oedema develops early in cardiac arrest, with failure of the energy dependent Na^+/K^+ ion exchange pump leading to influx of Na^+ and water into the cells and to K^+ efflux, depolarisation and Ca^{2+} influx. In an animal study (Fischer et al., Magnetic Resonance Imaging, 1995) including 10 cats in whom CA was induced for 15 minutes (followed by attempted resuscitation), MRI evidence of cerebral oedema was evident during CA (i.e. within 15 minutes of arrest onset).

Secondary brain injury begins once CBF is restored. Injury occurs through multiple mechanisms, including molecular shifts, release of neurotransmitters, activation of the innate immune system (including the release of cytokines which increase blood-brain barrier permeability, leading to vasogenic oedema). Restoration of flow is heterogenous and there is a correlation between sites that are most likely to suffer from a perfusion deficit and the areas of the brain that are most frequently injured (striatum, hippocampus, amygdala, thalamus). The combination of cytotoxic and vasogenic cerebral oedema may lead to intracranial hypertension and a fall in cerebral perfusion pressure. There is some early study data suggesting that invasively measuring and targeting ICP in post-CA patients may improve neurological outcomes, however Sandroni et al. consider this to be an area that requires 'considerable' further study, prior to making any management recommendations.

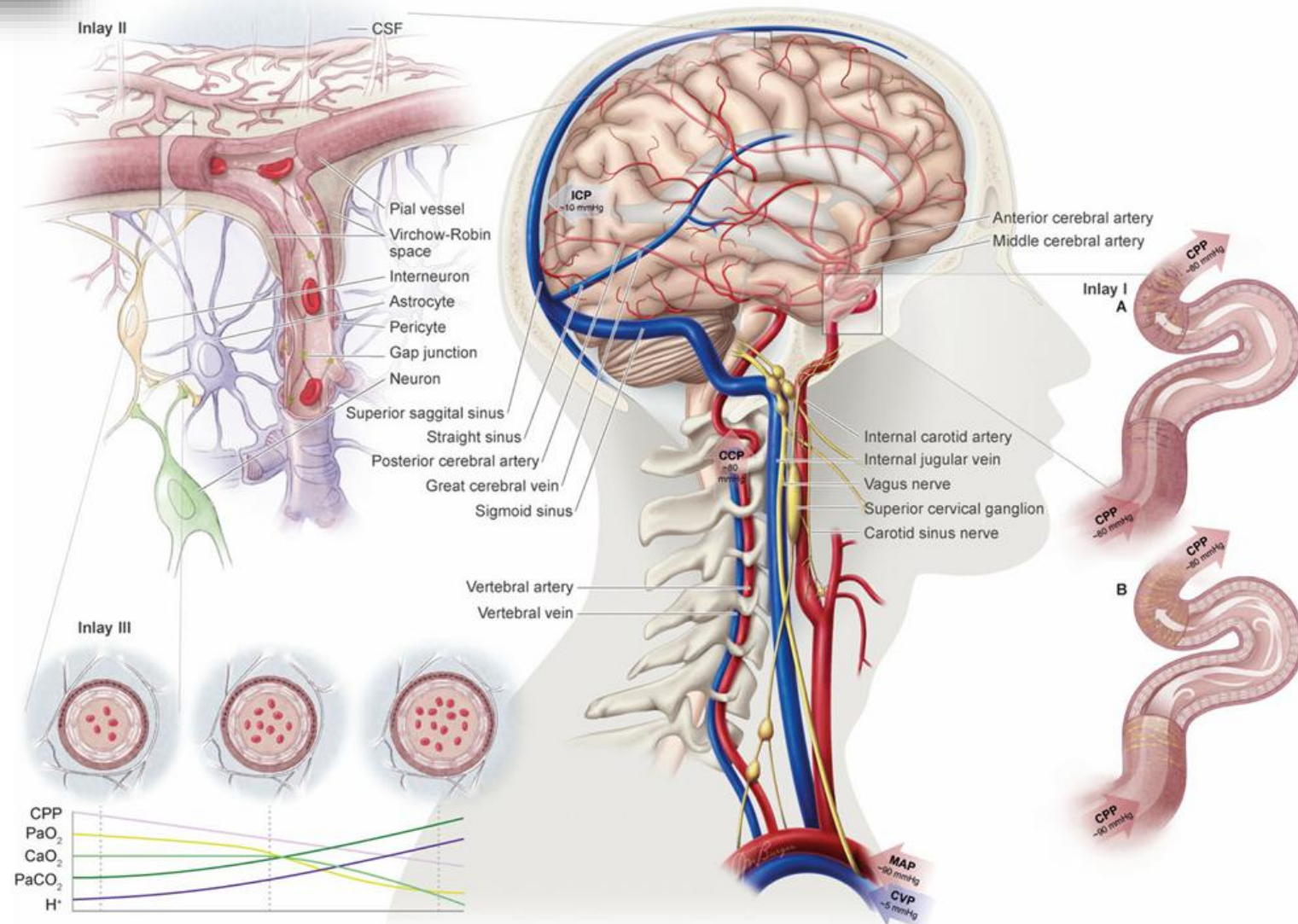
In the hours following ROSC there appears to be a hypoperfusion phase with CBF dropping by ~50%. This is associated with a commensurate decrease in cerebral oxygen demand. Patients in whom brain tissue hypoxia is detected via an intra-parenchymal micro-catheter (typical cut-off is $\text{PbtO}_2 < 20\text{mmHg}$) exhibited greater levels of neuronal injury biomarkers.

This figure (taken from Sandroni et al., ICM, 2021) shows outcomes following ROSC in 939 patients included in the TTM trial.

Integrative regulation of human brain blood flow

Christopher K. Willie¹, Yu-Chieh Tzeng², Joseph A. Fisher³ and Philip N. Ainslie¹

- Changes in local conditions can result in local changes in arterial tone (principally in the pial arteries in the subarachnoid space), allowing for regional modulation of flow.
- Systemic hypertension is countered with vasoconstriction, to protect the brain by preventing a sharp rise in ICP.
- Systemic hypotension is countered with vasodilatation, in order to maintain CBF and oxygen delivery.
- Exactly which vessels contribute (and to what extent) is debated.



Factors influencing cerebral blood flow

PaCO_2 exerts influence throughout the cerebrovasculature, from the large extra-cranial neck vessels to the small parenchymal vessels. A rise in PaCO_2 (and fall in extracellular pH) results in a rise in CBF (through vascular smooth muscle relaxation), and a fall in PaCO_2 (and a rise in extracellular pH) results in a fall in CBF. A fall in PaO_2 (below 50mmHg/6.7kPa) is associated with an increase in CBF, however the effect is blunted if there is coexisting hypocapnia (and is exacerbated if PaCO_2 rises as PaO_2 falls). The effect may be due to low DO_2 as opposed to low partial pressure of oxygen, as there is data that suggests a reduction in haematocrit can also result in a rise in CBF, perhaps via this mechanism. Whilst all (or if not all then at least a great many) cerebrovascular arteries are affected by changes in the arterial blood gases, the vessels which appear to exert the greatest impact on manipulation of CBF are the pial arteries (a network of arteries branching from the 'main' cerebral arteries, sitting within the sub-arachnoid space). These vessels are exposed to local conditions and therefore can modulate regional blood flow.

The site of modulation of arterial tone to buffer against systemic blood pressure changes appears to be debated. In this review article Willie et al. argue that large arteries proximal to the pial arteries (including the neck vessels) play an important role. The authors argue that it is possible that neck vessels may increase resistance by narrowing at tortuous segments, as this will induce a greater degree of turbulence (narrowing a tortuous vessel with turbulent flow will create a greater change in resistance than a comparable narrowing of a straight vessel with laminar flow).

It is possible that where changes in SBP and changes in PaCO_2 demand compensation in the same direction, a gross abnormality in one would prevent buffering against the other. For example, if SBP is already very low, then cerebral vessels may already be maximally dilated, such that a rise in PaCO_2 does not result in any further vasodilatation.

There is also direct autonomic innervation (both adrenergic and cholinergic) of the cerebral vasculature. Excision of sympathetic ganglions results in increased CBF. There is evidence that sympathetic control of large arteries plays a role in buffering against rises in SBP. Experiments using drugs to block the sympathetic ganglia or CNS adrenoceptors (for example with the alpha-blocker phentolamine) reduces the body's ability to prevent a rise in CBF in the face of a rise in MAP (for example, as induced with an infusion of noradrenaline). Interpretation of these experiments is challenging due to the difficulty in untangling any given drug's cerebral and systemic effects. There are also extensive parasympathetic nerve fibres that connect to the proximal large arteries, however, at the time of this review (2014) their role had not been investigated exhaustively.

PHYSIOLOGICAL REVIEWS

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Cerebral Blood Flow and Oxygen Consumption in Man

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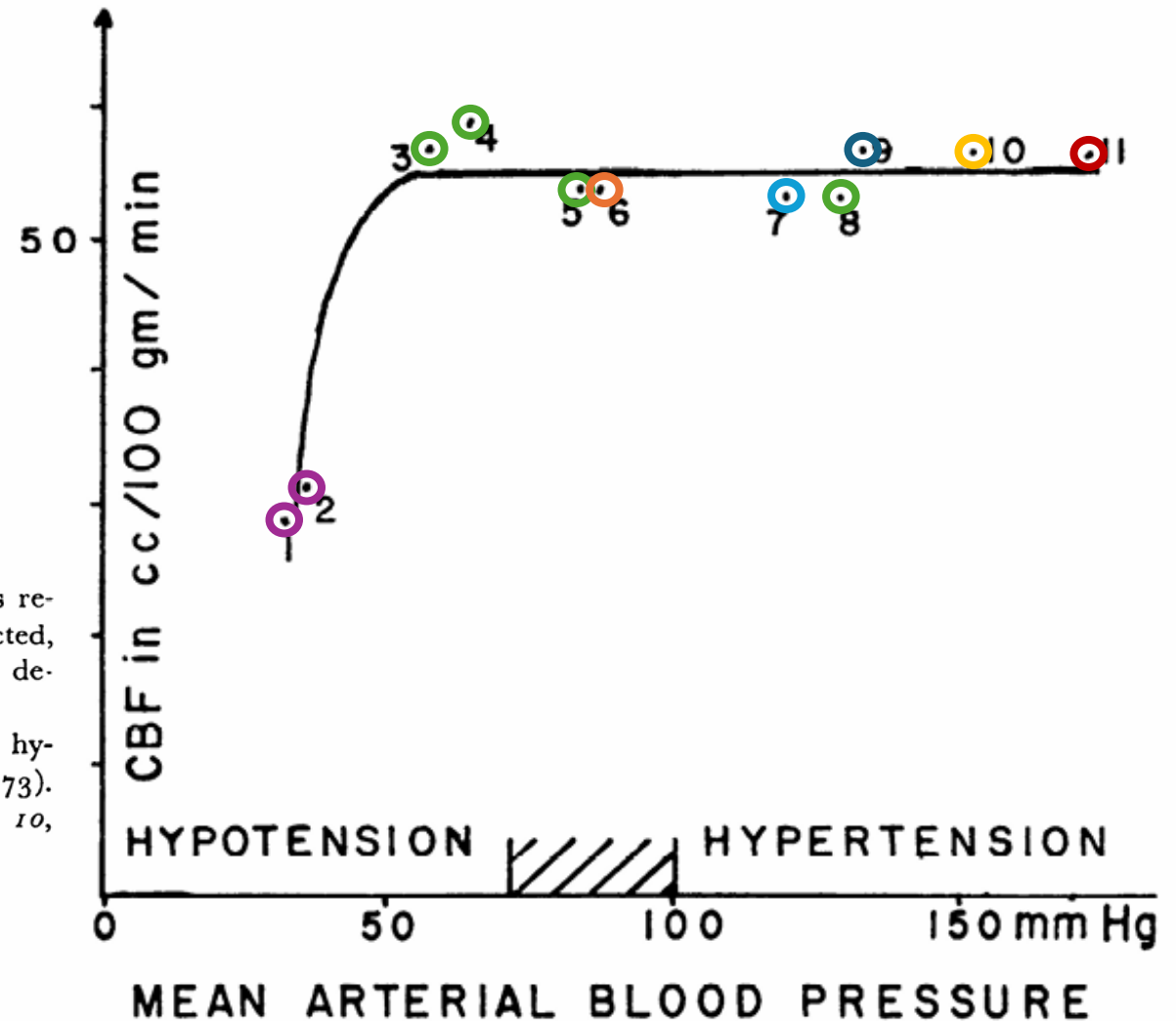


FIG. 1. Cerebral blood flow and blood pressure. Mean values of 11 groups of subjects reported in 7 studies have been plotted. Various acute and chronic conditions have been selected, characterized by a change in blood pressure. In all, this figure is based on 376 individual determinations.

1 and 2, Drug-induced severe hypotension (81). 3 and 4, Drug-induced moderate hypotension (206). 5 and 6, Normal pregnant women and normal young men (206, 173). 7, Drug-induced hypertension (230). 8, Hypertensive toxemic pregnancy (206). 9, 10, 11, Essential hypertension (229, 131, 228).

Cerebral autoregulation

The concept of autoregulation of CBF (that the healthy brain can maintain a fixed CBF over a wide range of MAPs) came out of work in the late 1950s by Lassen. In this paper he reviewed data from 7 previous studies, and derived 11 cohorts of patients, and for each cohort compared the cohorts mean CBF (indexed for brain weight) with the cohorts mean MAP. All of the cohorts had broadly similar (and 'normal') means for CBF despite having wildly different means for MAP, with the exception of cohorts 1 and 2, which had the lowest mean values for both. Cohorts 1 and 2 are both taken from one paper (Finnerty, Journal of Clinical Investigation, 1954), from the mid-1950s, and is common for papers published at this time the methods section is less unambiguous than would be required to pass peer review now. It appears that in a subset of their patients they gave an infusion of hexamethonium (neuronal nACh receptor antagonist) whilst they were laying on a tilting table, until inducing neurological signs such as 'staring' and 'confusion', then adjusted the angle of the table (and hence the postural component of blood flow) to maintain this altered neurological state (avoiding both 'alertness' and unconsciousness). MAP was measured via cannulation of the femoral artery. CBF appears to have been estimated by a technique that involved sampling arterial and jugular venous blood and looking at differences in O_2 and CO_2 (similar to the Fick method for estimating cardiac output). They found that clinical neurological signs began when CBF fell below $\sim 35\text{ml}/100\text{g}/\text{min}$, and that this occurred at different levels of MAP (at higher MAPs in patients with a history of 'malignant hypertension') and different levels of ΔMAP .

One criticism of this graph is that points 3 and 4 (or perhaps only point 3, from reading the original reference – McCall, American Journal of Obstetrics and Gynaecology, 1956 – I am not immediately certain) represent measurements made in pregnant women treated with a potent vasodilator (veratrum viride), such that whilst MAP fell, there was likely to have been simultaneous marked cerebral vasodilatation, a drop in cerebrovascular resistance and this would have augmented CBF. Therefore, an insult that reduced MAP to levels $\sim 60\text{-}65\text{mmHg}$ might result in reduced CBF if that insult did not simultaneously reduce cerebrovascular resistance.

Importantly therefore this is not demonstrating that individuals exhibited a fixed CBF across different blood pressures, but rather many different individuals with different blood pressures, in different clinical contexts, exhibited similar CBF (with only one study reporting a reduction in CBF below 'normal').

Autoregulation of cerebral blood flow: influence of the arterial blood pressure on the blood flow through the cerebral cortex

A. MURRAY HARPER

From the University of Glasgow, Wellcome Surgical Research Laboratory, Bearsden Road, Bearsden, Glasgow

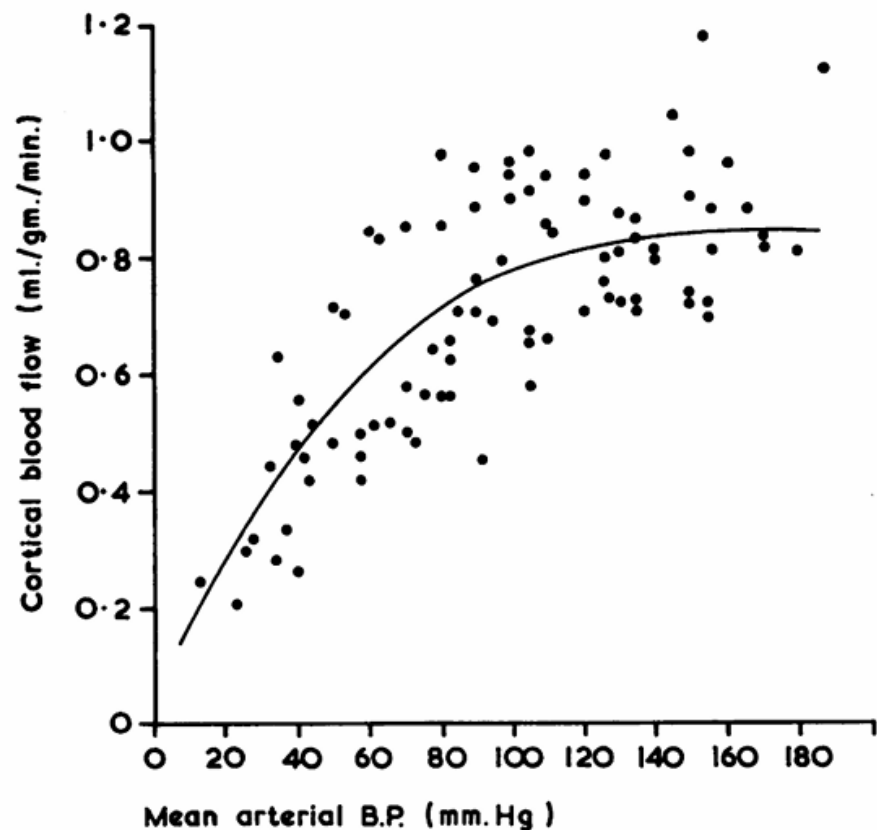


FIG. 1. *Response of cortical blood flow to changes in mean arterial blood pressure in normocapnic animals. Line is best polynomial fit.*

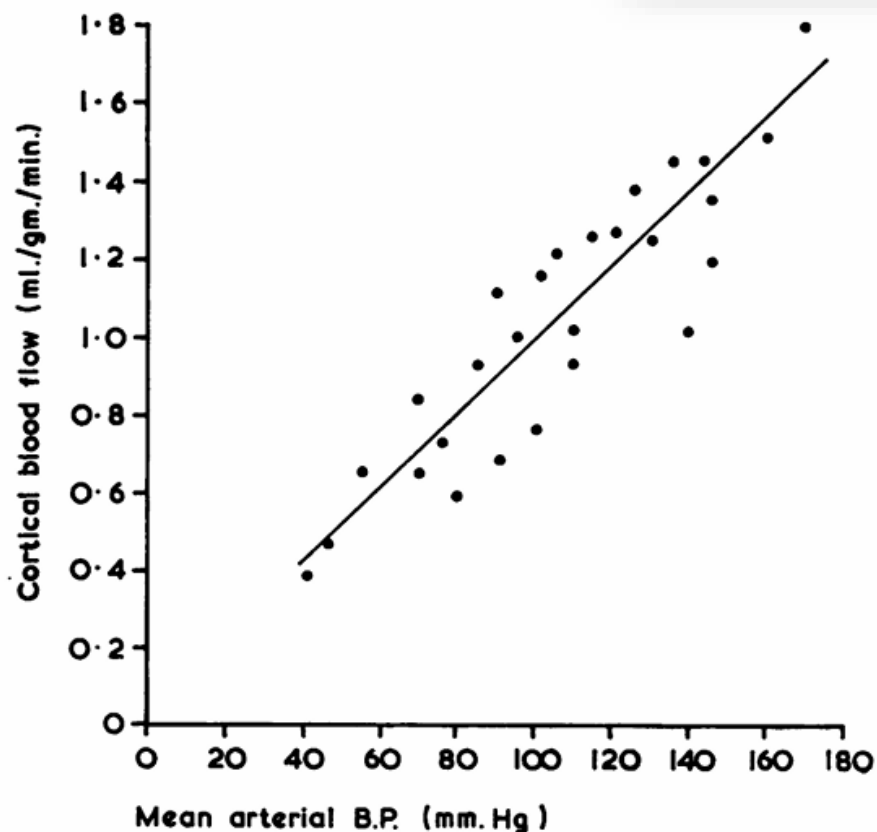


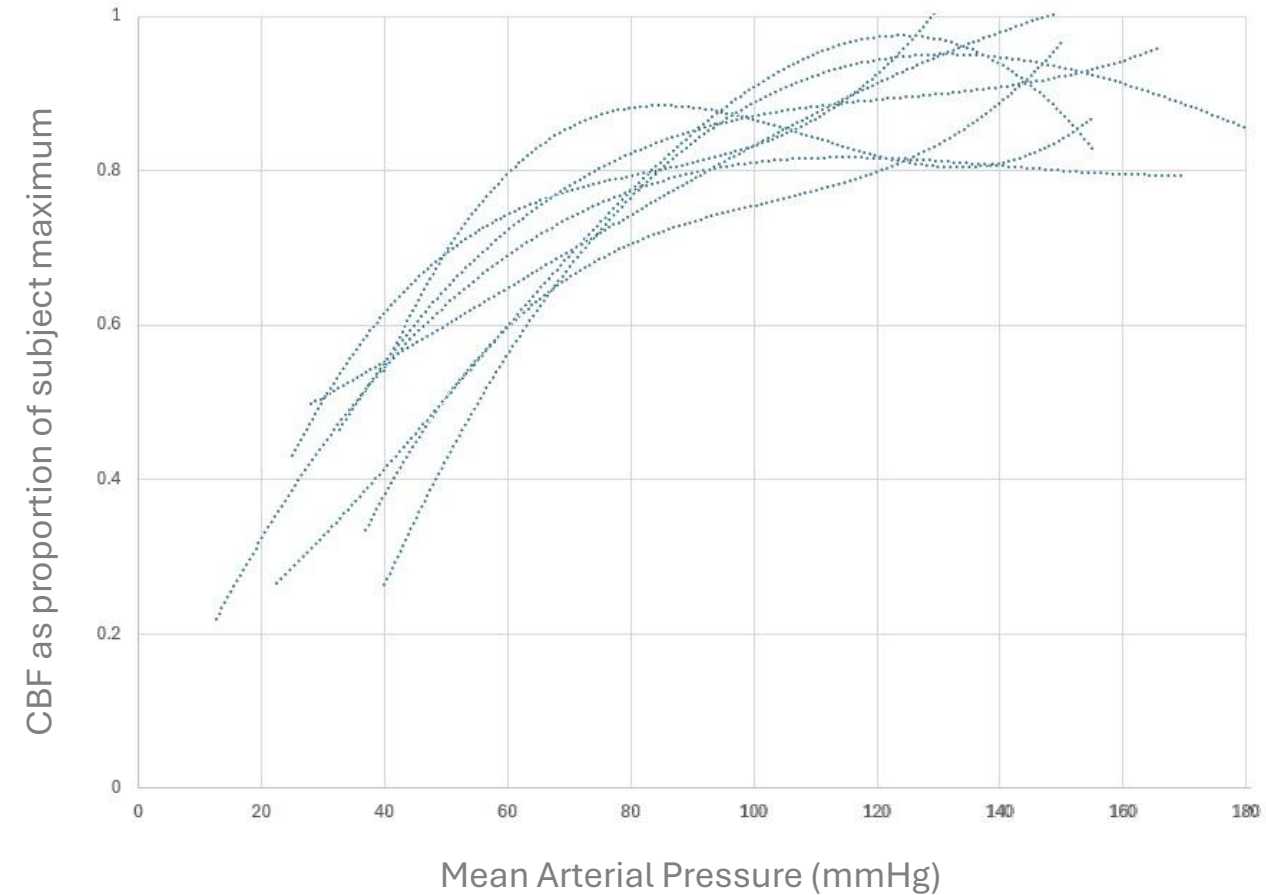
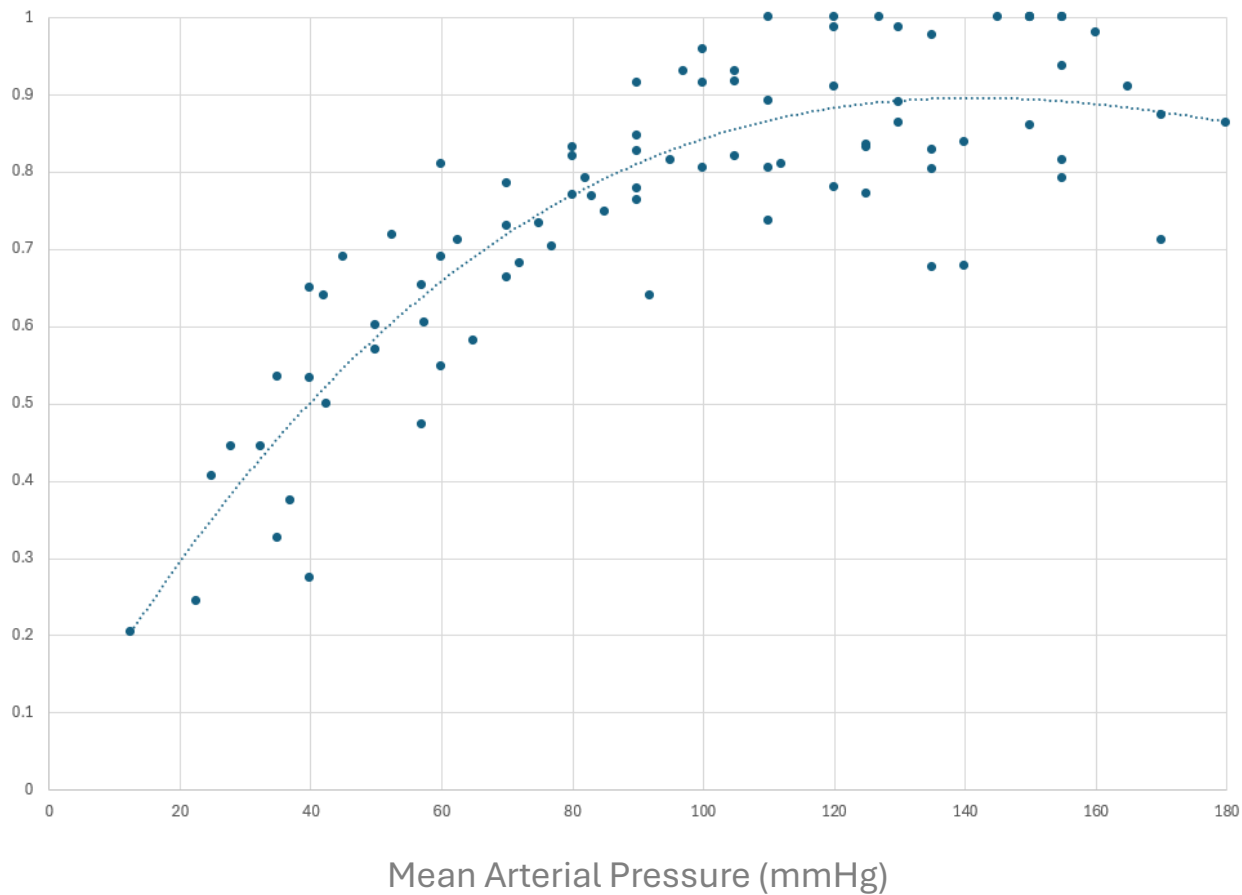
FIG. 2. *Response to cortical blood flow to changes in mean arterial blood pressure in hypercapnic animals. Line is calculated linear regression.*

In this paper by Harper from 1966, 117 measurements were made from 12 anaesthetised dogs. Subjects underwent surgical trephine and a Geiger counter was placed such that it could measure the parietal cortex, and then Krypton saturated Dextran was infused into the cerebral circulation. CBF was estimated by measuring the drop in radioactivity over time as assessed by the Geiger counter. In 8 dogs normocapnia (PaCO_2 30-40mmHg, 4-5.3kPa) was achieved through adjustments in ventilation, and following this sequential venesection was performed with measurements of CBF and MAP made at intervals (figure 1). In 4 dogs the arterial CO_2 was elevated to 68-86mmHg (9.1-11.5kPa) and the same technique used to assess the relationship between MAP and CBF under conditions of hypercapnia (figure 2).

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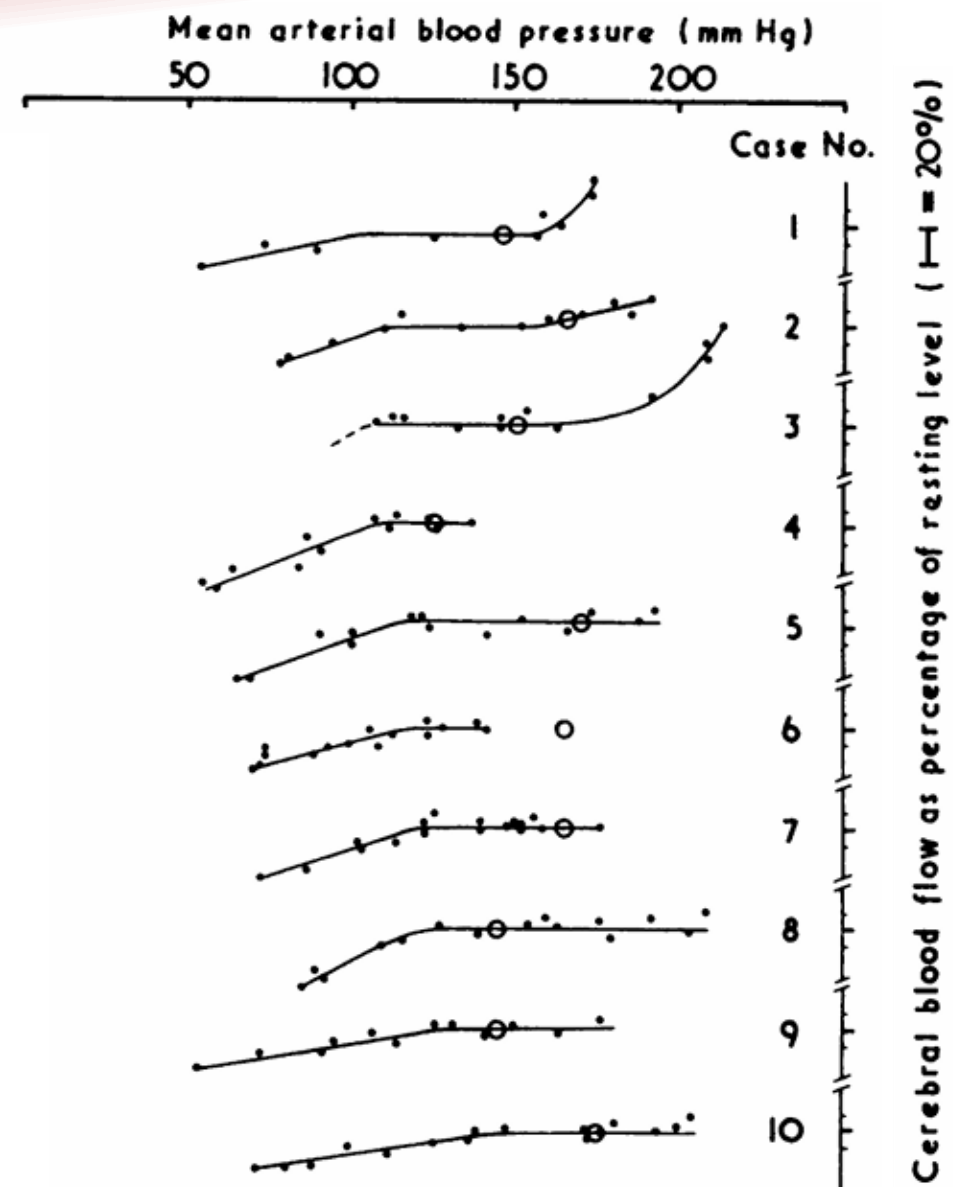
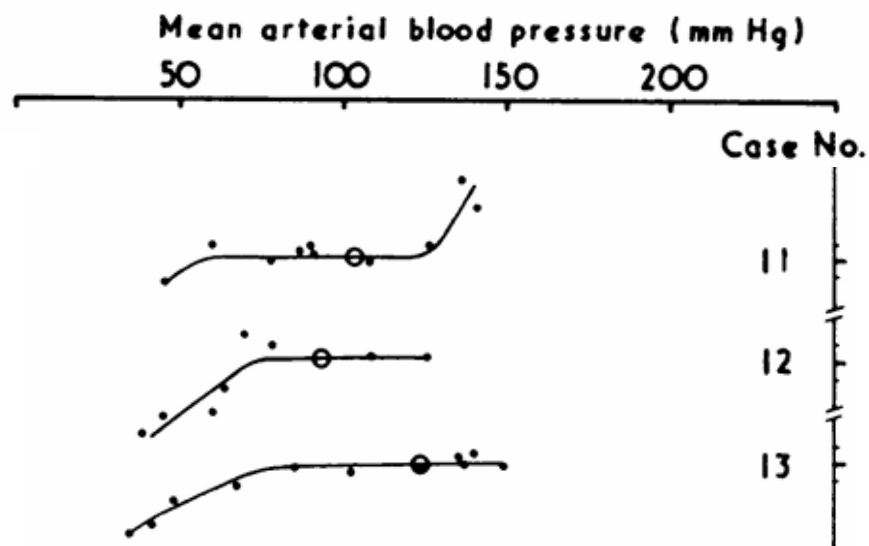


Data points for individual subjects are provided within tables. If we look at each estimate of CBF and index it for the greatest CBF for each subject (the graph on the left), then we can see that there is a trend for CBF to start to drop off for MAPs below 80mmHg. We can produce 3rd order polynomial trendlines for each individual subject and then overlay these to see the graph on the right.

PAPERS AND ORIGINALS

Autoregulation of Brain Circulation in Severe Arterial Hypertension

S. STRANDGAARD, J. OLESEN, E. SKINHØJ, N. A. LASSEN

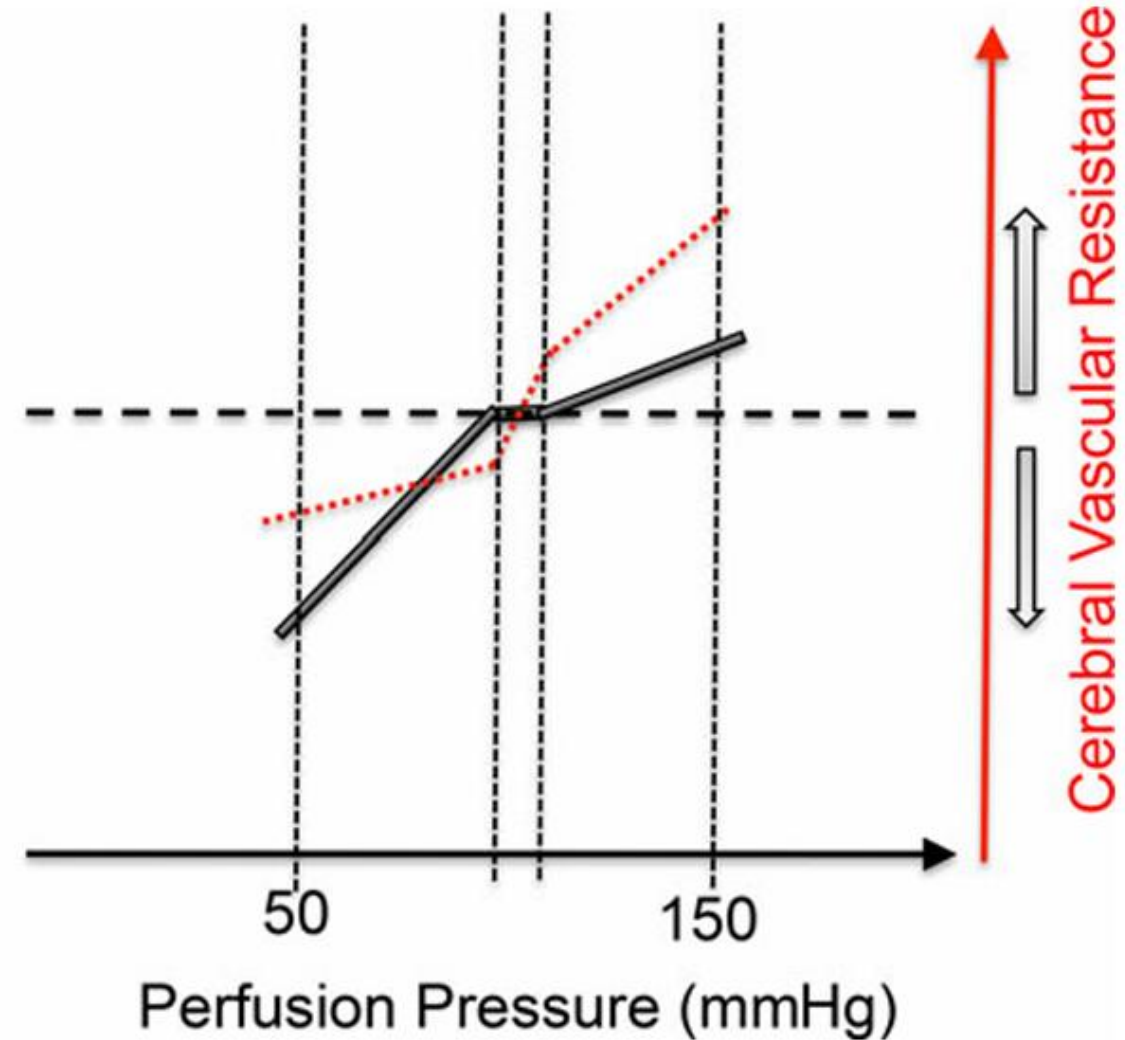
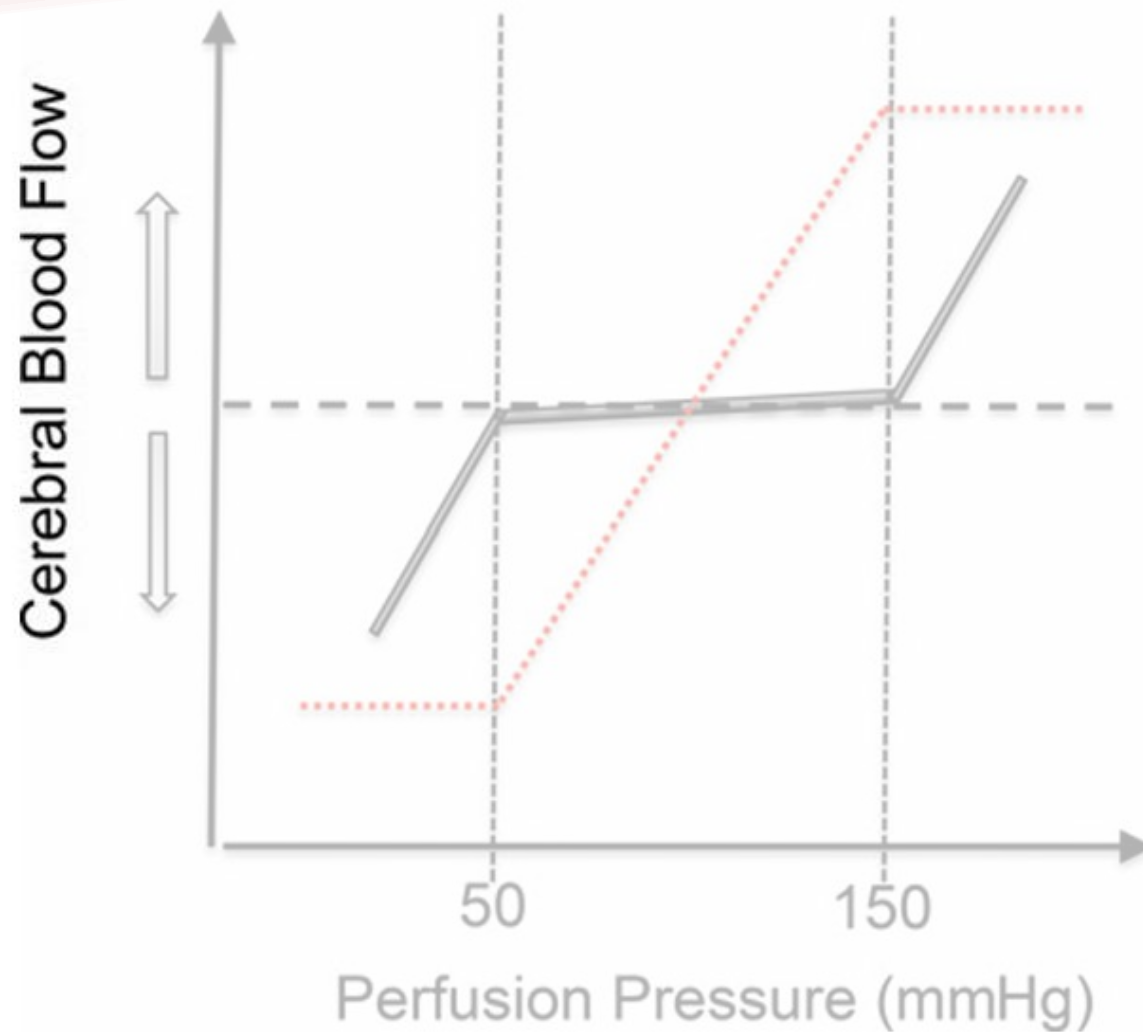


In this study by Strandgaard et al. 13 patients were studied, 10 of whom had chronic hypertension (baseline systolic BP 160-250mmHg, baseline diastolic BP 110-145mmHg) with hypertensive complications (all had hypertensive eye disease and abnormal ECGs, whilst SCr ranged from ~90-180micromol/L with many having proteinuria). The three remaining patients (patients 11-13) had normal or mildly elevated baseline BP (130/90, 120/80 and 170/105 respectively). CBF was estimated by measuring the arteriovenous oxygen difference and blood pressure was manipulated by infusion of angiotensin amide (to raise BP) and/or trimethaphan camsylate (neuronal nACh receptor antagonist). Scatter plots were created for individual patients and lines of best fit drawn by visual assessment (as opposed to having been calculated).

The authors found that for patients with hypertension there was a lower inflection point at ~120mmHg. In the patients without hypertension this inflection point was ~70mmHg. In addition the authors assessed the point at which patients exhibited neurological symptoms/signs attributed to brain hypoxia (discomfort, dizziness, sleepiness, nausea). On average these symptoms/signs appeared at 68mmHg (when CBF dropped to 73% of resting level). In the 3 control patients these symptoms/signs arose at an average of 40mmHg.

Integrative regulation of human brain blood flow

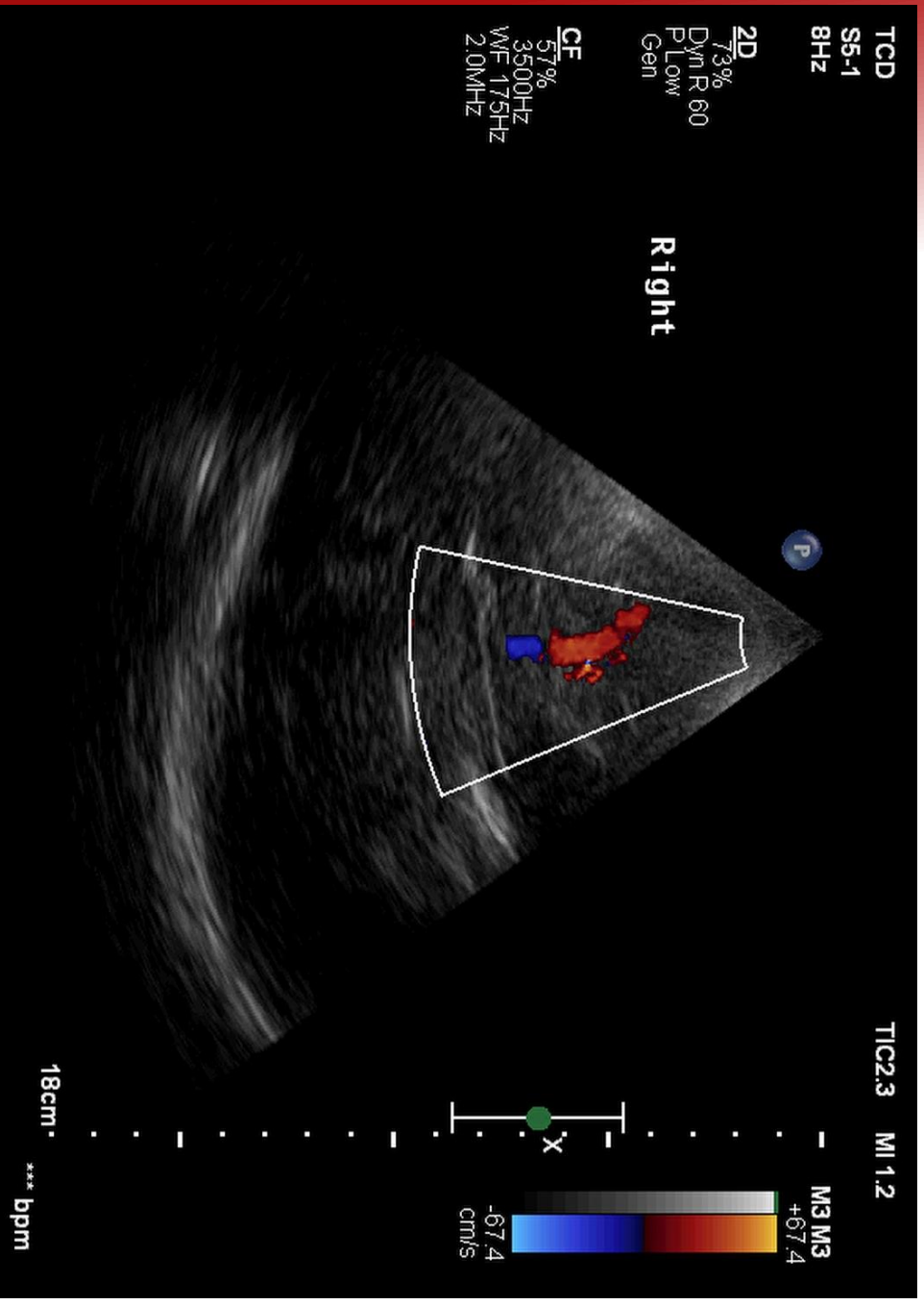
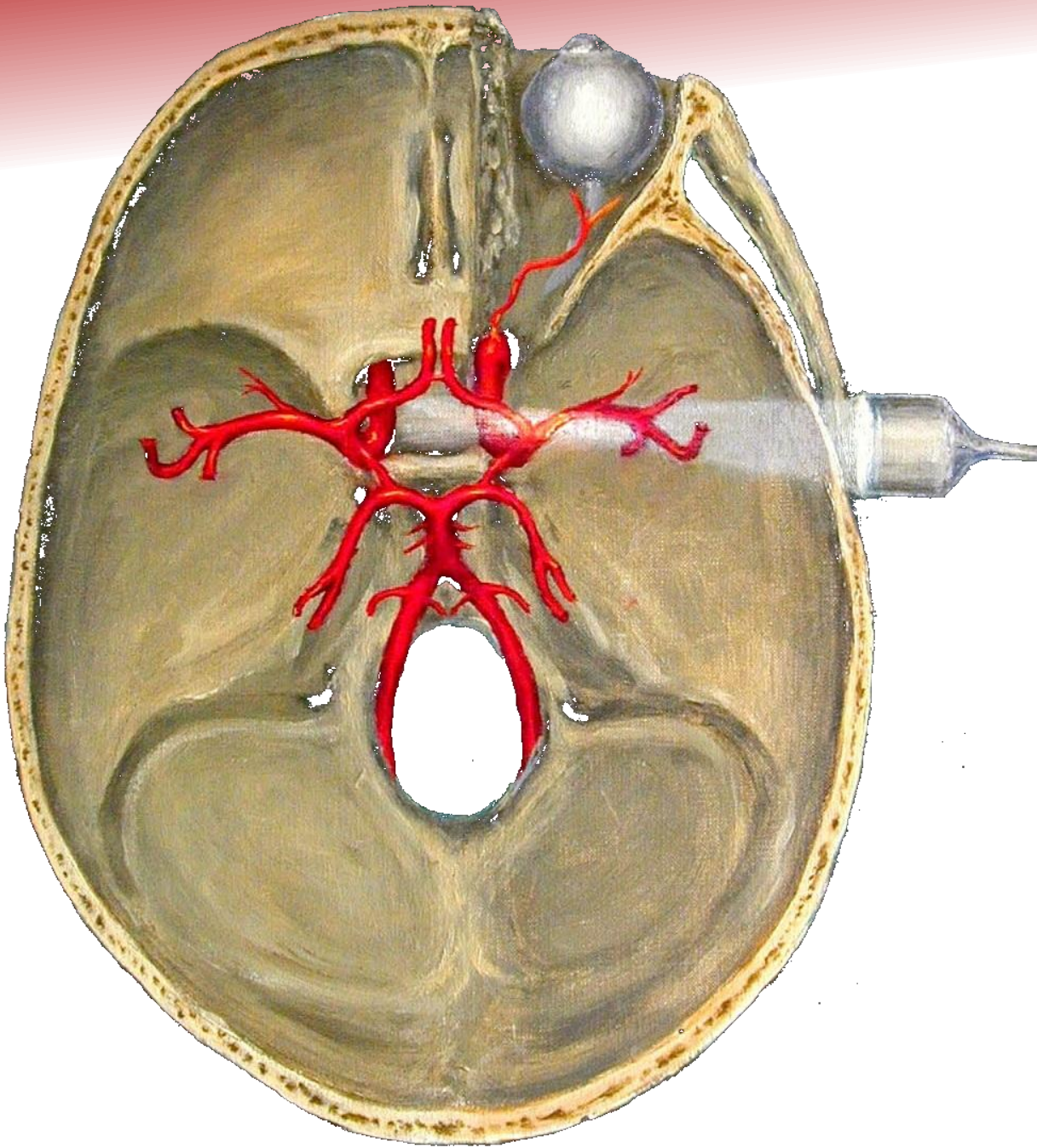
Christopher K. Willie¹, Yu-Chieh Tzeng², Joseph A. Fisher³ and Philip N. Ainslie¹



The graph on the left is widely taught as representing autoregulation of CBF in health. However, Willie et al. argue that this representation is misleading, and that studies performed since this model was first proposed suggest: the plateau is narrower than traditionally represented, with a lower inflection point that is far higher; CBF below the lower inflection point is more pressure dependent than flow above the upper inflection point (i.e. CBF is more sensitive to low BP than to high BP).

Willie et al. go on to provide a number of reasons why our current model is likely to remain imperfect: it is difficult to safely produce a wide range of different blood pressures within a single subject; when TCD is used to estimate CBF there is an assumption that vessel diameter is unchanged between assessments, whilst there is evidence that this is not always the case (large vessels – those assessed with TCD – also alter their calibre in the face of large changes in MAP); when blood pressure is manipulated by drugs, then the changes in systemic vascular tone exploited to bring about the change in MAP are likely to also effect the cerebral vasculature (i.e. both sides of the equation are being manipulated and the observed buffering cannot solely be attributed to autoregulation); most studies do not allow for the fact that PaCO_2 may change across the course of the experiment.

With respect to cerebral autoregulation (CA), this paper goes on to discuss two terms that appear in the relevant literature, namely static CA and dynamic CA. In their opinion there is no reason to believe that these two terms are describing different physiological phenomena but rather reflect a difference in measurement techniques. Static CA refers to the relationship described by comparing a number of measurements made at distinct time points. The availability of TCD allows for changes in flow to be detected beat-to-beat, with concurrent MAP measurements via invasive arterial lines. This allows for a far higher sampling rate and when experiments are performed in this way, it is referred to as dynamic CA. These later studies employing TCD suggest that there is a short lag between changes in MAP and recovery of CBF, but that earlier studies lacked the temporal resolution to detect this lag.

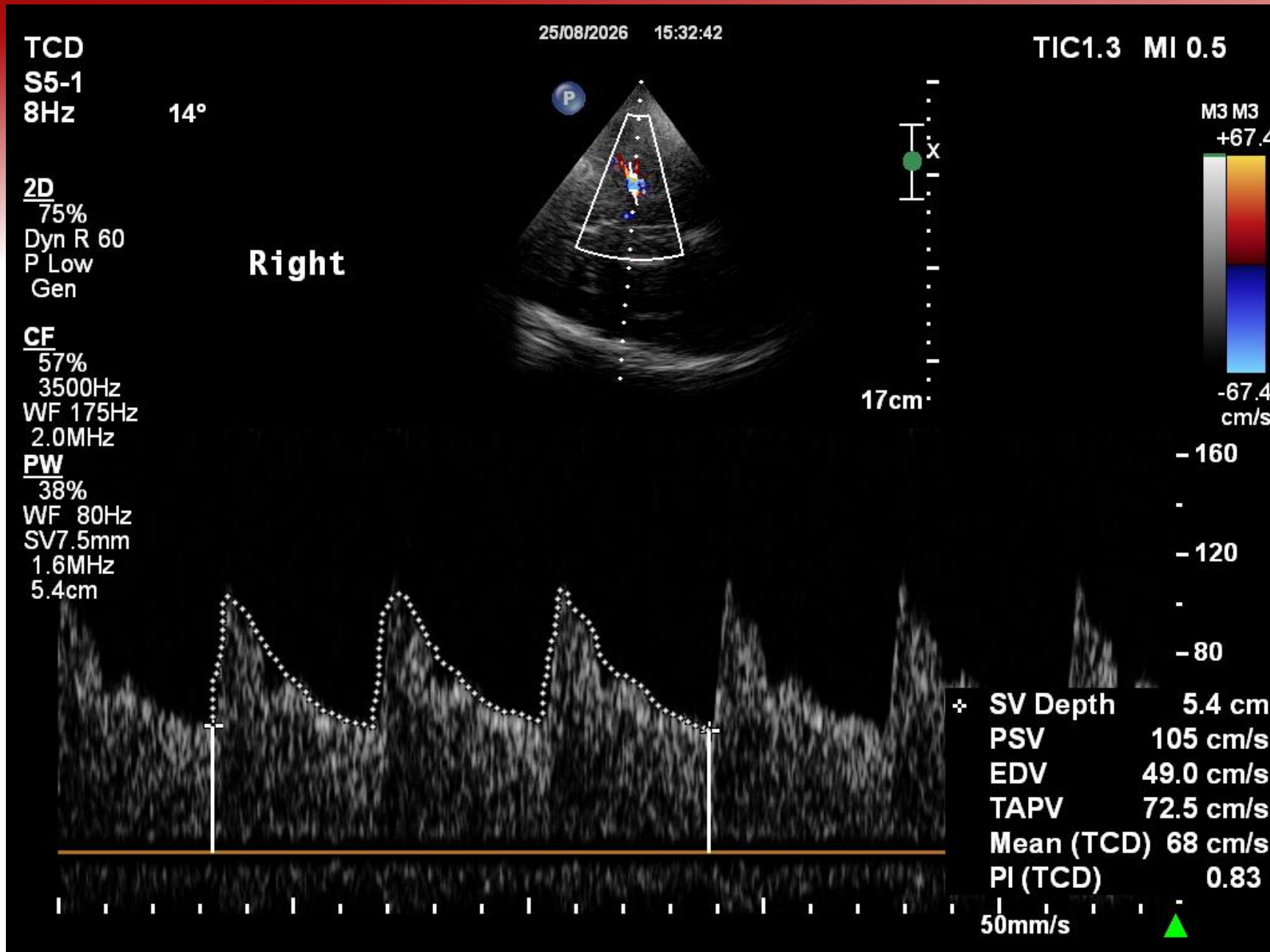


Trans-Cranial Doppler assessment of cerebral blood velocities

We know that CBF can vary, that brain injury can cause disordered regulation CBF and extremes of CBF can lead to secondary injury. How can we use ultrasound to best understand our patients CBF?

First, we need to revise the ('normal') anatomy of the major intra-cranial arteries. The internal carotid arteries arise from the common carotid arteries. The cervical segment (C1) is extra-cranial. The petrous segment (C2) enters the skull through the foramen lacerum (bordered by the sphenoid, temporal and occipital bones). Segments C3-C6 pass within the skull, and the origin of the posterior communicating artery marks the end of segment C6 and the start of the terminal (or communicating) segment (C7) which bifurcates into the middle cerebral artery and the anterior cerebral artery). The most proximal segment of the middle cerebral artery is the sphenoidal segment (M1) which runs laterally along the sphenoid bone. The M1 segment is orientated towards the US probe (when imaging from the temporal window). The MCA has 3 further segments beyond M1 (the insular segment, M2, the opercular segment, M3, and the terminal or cortical segment, M4). The A1 segment of the anterior cerebral artery extends until the origin of the anterior communicating artery, beyond which is the A2 segment. In the posterior circulation, the vertebral arteries typically arise from the subclavian arteries and travel superiorly passing through the transverse foramen of each cervical vertebra from C6 up, entering the skull through the foramen magnum. The vertebral arteries join to form the basilar artery which terminates when it bifurcates into the two posterior cerebral arteries. The posterior communicating arteries arise from the posterior cerebral arteries, and the point at which they arise marks the boundary between the P1 and P2 segments of the posterior cerebral arteries.

The still on the left is taken from a 2D with colour clip from a healthy volunteer. The probe is held over the right temporal window, in a transverse orientation and with the orientation marker pointing anteriorly. The clip has been rotated to match the orientation of the diagram to the right. In the far field the left temporal bone is visible. Red colour flow is seen within the proximal M1 segment of the right MCA, whilst blue colour flow is seen within the proximal A1 segment of the right ACA.



TCD measurements:

- Peak Systolic Velocity (PSV)
- End-Diastolic Velocity (EDV)
- Time-Averaged Peak Velocity (TAPV)

Calculations:

- $\text{Mean} = \text{EDV} + (\text{PSV} - \text{EDV}) / 3$
- $\text{PI} = (\text{PSV} - \text{EDV}) / \text{Mean}$
- Velocity $\neq$ Flow

This PW Doppler graph is from the same healthy volunteer. We can see that a small amount of angle correction has been applied (14 degrees). The sample volume itself has a length of 7.5mm. The centre of the sample volume is 5.4cm from the probe. Sample volume depth is displayed as flow assessment is performed multiple times along the length of the vessel when assessing for vasospasm in patients who have suffered a subarachnoid haemorrhage.

It is important to remember that velocity does not equal flow, as we have not measured the calibre of the vessel (in order to ascertain its cross-sectional area).

Transcranial Color-Coded Sonography of the Basal Cerebral Circulation

Reference Data From 115 Volunteers

P.J. Martin, MA, MRCP; D.H. Evans, PhD, FInstP; A.R. Naylor, MD, FRCS

Artery	Velocity	Mean Velocity, cm/s (95% CI)			P		
		20-39 y	40-59 y	>60 y	20-39 vs 40-59 y	40-59 vs >60 y	20-39 vs >60 y
MCA	Peak	113 (109-116)	106 (101-111)	92 (88-96)	<.05	<.0001	<.0001
	Mean	74 (71-76)	72 (69-76)	58 (55-61)	NS	<.0001	<.0001
	ED	51 (49-53)	47 (45-50)	35 (33-37)	<.05	<.0001	<.0001

Artery	Age, y	Peak, cm/s (95% CI)			Mean, cm/s (95% CI)		
		Men	Women	P	Men	Women	P
MCA	20-39	108 (103-113)	115 (110-120)	<.05	70 (66-74)	77 (73-80)	<.05
	40-59	99 (94-104)	112 (105-120)	<.005	66 (62-69)	78 (73-83)	<.0005
	>60	94 (89-100)	88 (82-94)	NS	58 (55-62)	57 (53-62)	NS

Artery	Pulsatile Index (95% CI)			P		
	20-39 y	40-59 y	>60 y	20-39 vs 40-59 y	40-59 vs >60 y	20-39 vs >60 y
MCA	0.84 (0.82-0.87)	0.81 (0.79-0.83)	0.97 (0.93-1.02)	<.05	<.0001	<.0001

Reference intervals were derived from 115 healthy volunteers by Martin et al. (Stroke, 1994). They found that (with respect to CBFV in the MCA): all velocities fall with age; pulsatility index is higher in older individuals (age >60 years); that for younger women (age <60 years) peak and mean velocities are higher than for men of a similar age (with no significant difference for older individuals).

These values have subsequently been simplified and repeated in subsequent review articles. For example, Blanco and Blaivas (Journal of Ultrasound Medicine, 2017) report the following reference intervals (not age or sex specific): PSV, 90-110cm/s; EDV, 35-55cm/s; mean, 55-80cm/s; PI, 0.81-0.97.

KCL Carotid

L12-3

23Hz

66°

2D

41%

Dyn R 56

P Low

HGen

CF

51%

2909Hz

WF 130Hz

4.0MHz

PW

10%

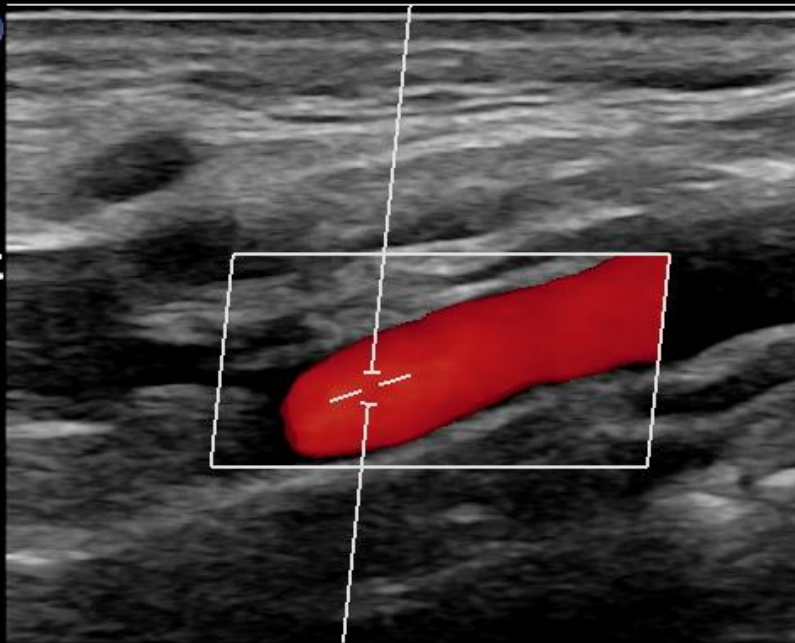
WF 40Hz

SV1.5mm

3.6MHz

1.8cm

Right



TIS0.2 MI 0.8

PSV -75.4 cm/s

EDV -32.2 cm/s

MDV -32.2 cm/s

RI 0.57

X2

M3 M3
+28.0

-28.0
cm/s

3.0cm

-80

-60

-40

Cerebral Vasospasm Diagnosis by Means of Angiography
and Blood Velocity Measurements *

K.-F. Lindegaard, H. Nornes, S. J. Bakke, W. Sorteberg, and P. Nakstad

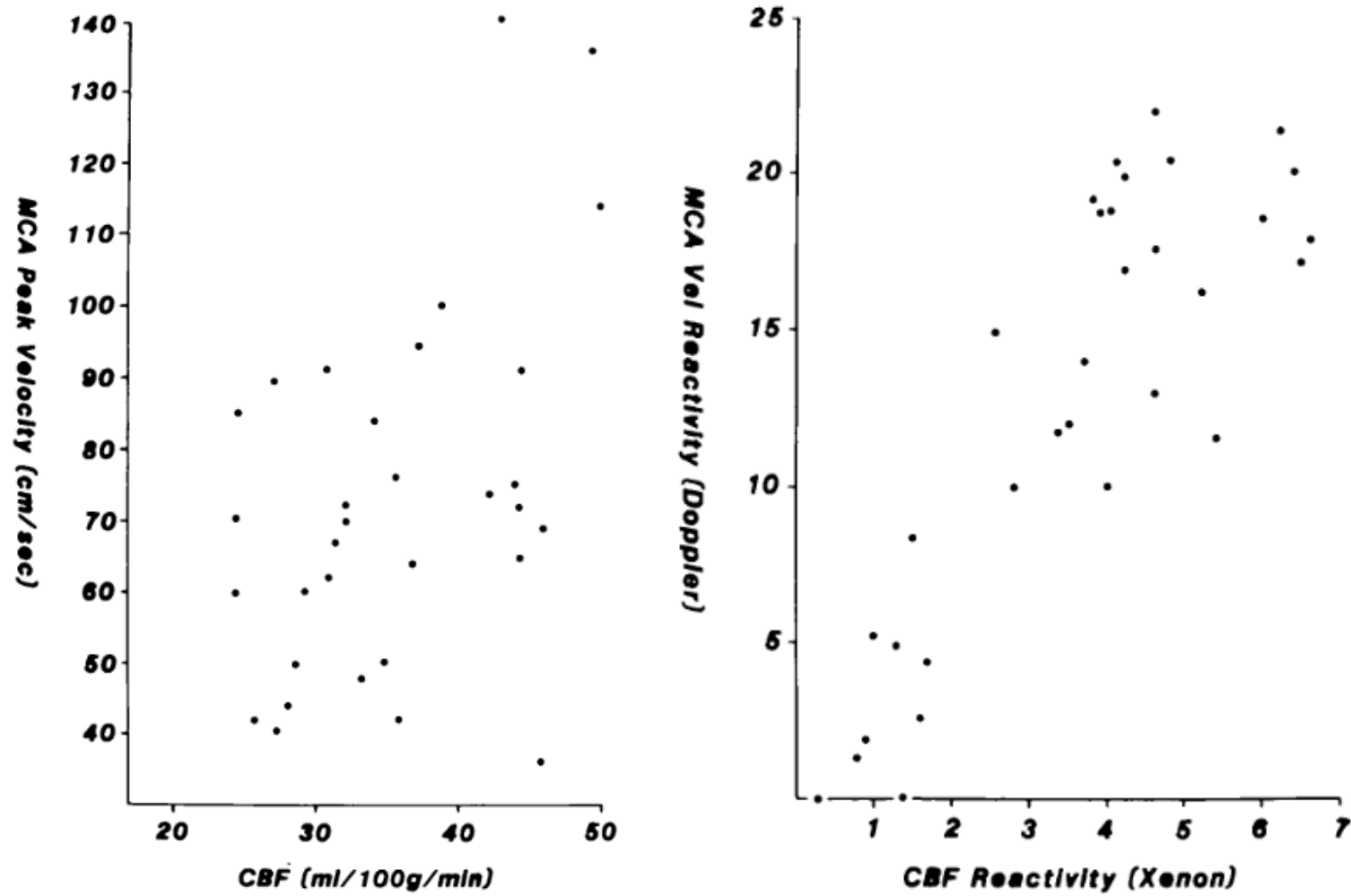
66mm/s

- Elevated intra-cranial velocities may represent vessel narrowing and increased resistance or hyperaemia (elevated flow).
- When monitoring for vasospasm in SAH, when velocities are elevated the velocity in the intra-cranial artery is compared to the velocity in the ipsilateral extra-cranial ICA.
- The ratio of mean velocities is calculated.

This technique of assessing the ratio of mean velocities was first described by Lindegaard et al. (Acta Neurochirurgica, 1989).

Transcranial Doppler Measurement of Middle Cerebral Artery Blood Flow Velocity: A Validation Study

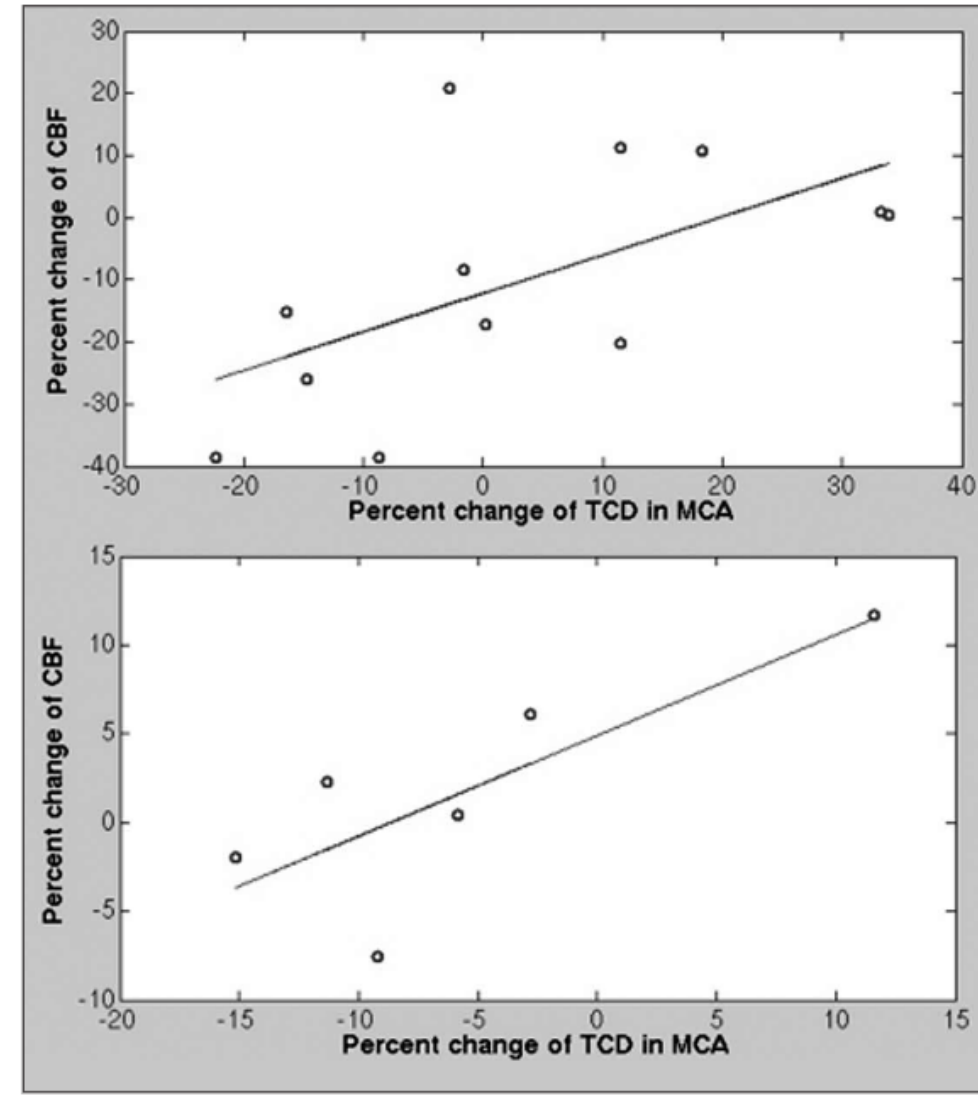
C.C.R. BISHOP, M.A., F.R.C.S., S. POWELL, B.Sc., D. RUTT, S.M.L.S.O., AND N.L. BROWSE, M.D., F.R.C.S.



Brain Blood Flow and Velocity

Correlations Between Magnetic Resonance
Imaging and Transcranial Doppler Sonography

Farzaneh A. Sorond, MD, PhD, Norman K. Hollenberg, MD, PhD,
Lawrence P. Panych, PhD, Naomi D. L. Fisher, MD



Trans-Cranial Doppler for the estimation of cerebral blood flow

Cerebral blood flow velocity (CBFV) does not equate to cerebral blood flow (CBF, volume/time). This is important because many relevant studies use CBFV as a surrogate for CBF. The correlation between CBFV and CBF (as assessed by a variety of techniques) has been studied by numerous authors. As might be expected the findings of each study are not always perfectly consistent, but it appears that whilst a correlation is present, it is far too weak for any point estimate of CBFV to be used as a point estimate of CBF.

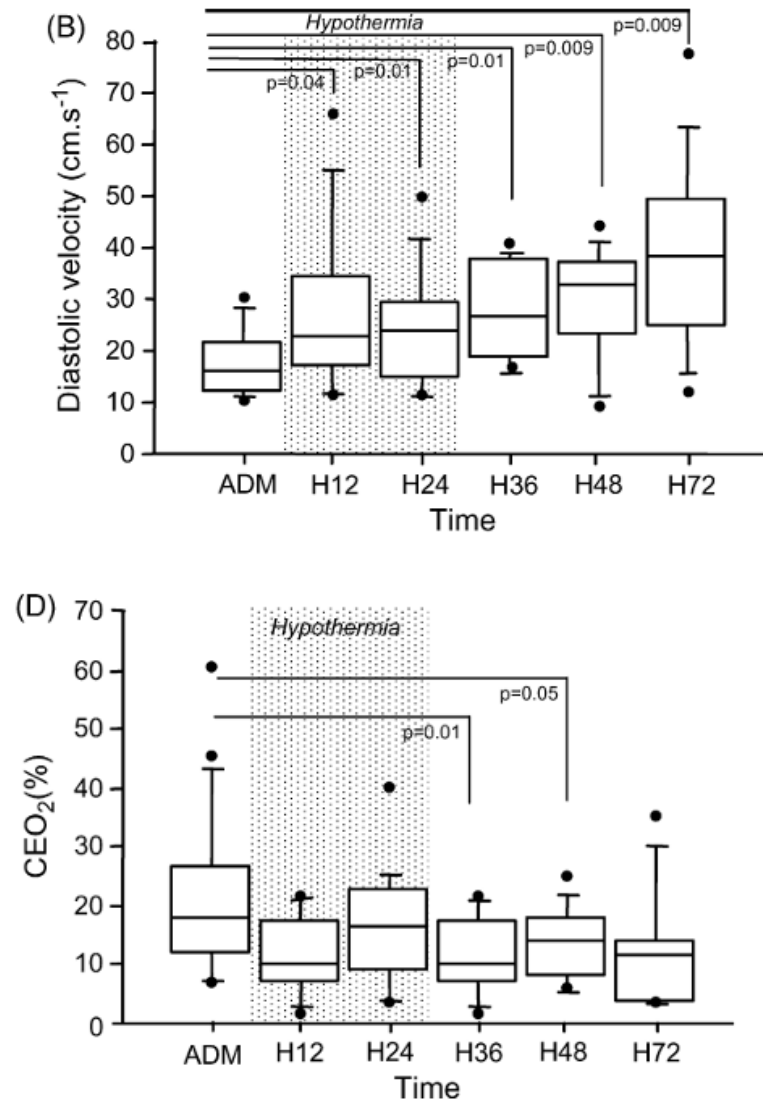
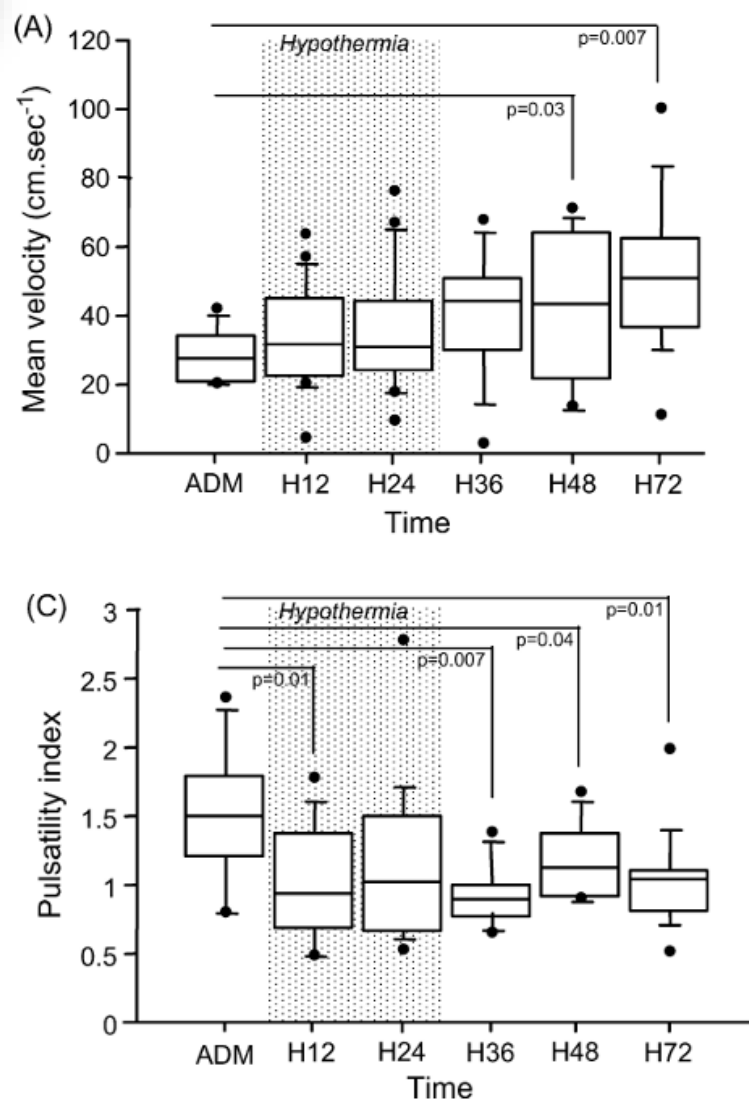
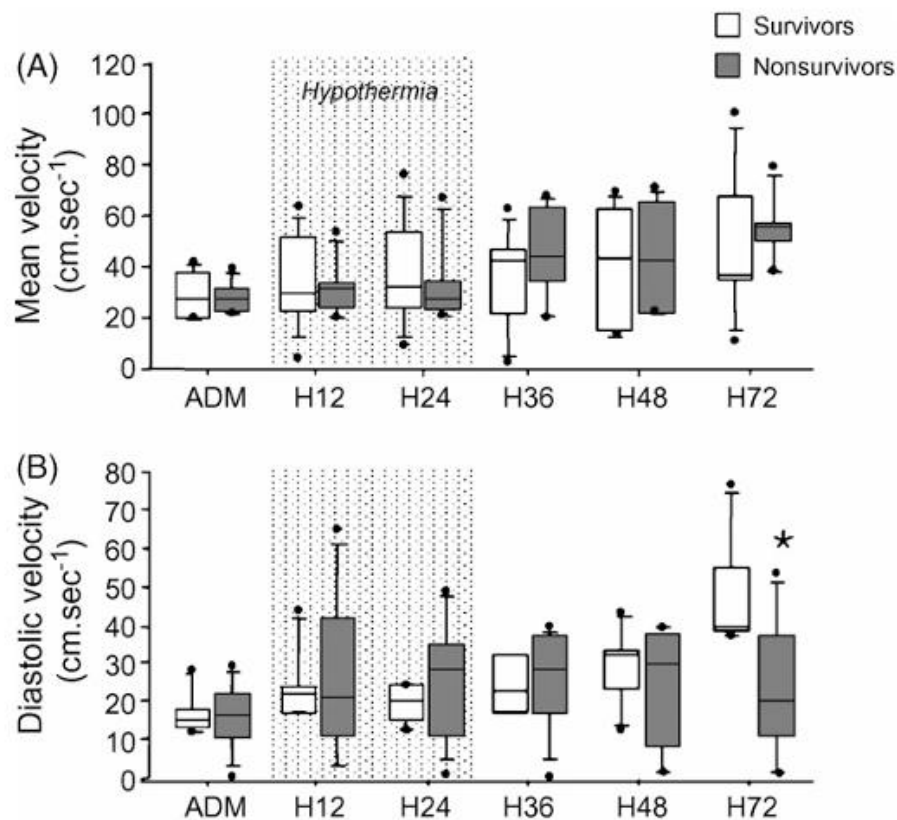
Bishop et al. (Stroke, 1986) studied 17 patients with cerebrovascular disease. TCD MCA PSV was compared with estimated CBF (patients received an intravenous injection of xenon, and then xenon clearance from the brain was measured, in a technique that is probably similar to thermodilution estimation of cardiac output). At rest estimated CBF ranged from 24-50ml/100g/min, whilst PSV ranged from 36-140cm/s. The correlation (demonstrated in the left-hand figure) was poor, with an r-value of 0.424. They then induced hypercapnia by asking patients to breathe a mixture of 95% air/5% CO₂, breathing this mixture until reaching a new steady state of etCO₂ (the resting and hypercapnia levels of etCO₂ are not reported). They then correlated the %Δ in PSV against the %Δ in estimated CBF and found that this correlation was much stronger (r=0.849, central figure). Of note, the %Δ in PSV ranged from 0-21, whilst %Δ in estimated CBF ranged from 0.3-6.6, i.e. the magnitude of the PSV %Δ was ~4-5x that of estimated CBF %Δ.

Sorond et al. (Journal of Ultrasound Medicine, 2010) studied 20 healthy elderly individuals (all non-smokers without diabetes), to assess the change in mean velocity (of right MCA) against change in estimated CBF (as assessed using two different MRI techniques, 2 patients excluded due to technical failures, 12 patients assessed using a gadolinium technique, 6 patients assessed using an Arterial Spin Labelling technique), before and after drinking 2 cocoa rich drinks every day for 7-14 days (imaging performed 2-4 hours after last drink). In this small dataset there was a moderate correlation between %Δ in mean velocity and %Δ in CBF (r=0.63 for gadolinium technique, right upper figure, r= 0.80 for ASL technique, right lower figure).

The small selection of papers I have studied on this topic suggest that it is unadvisable to use CBFV as an estimate of CBF between different patients, whilst using a change in CBFV to estimate change in CBF within a single individual is more reliable (although remaining far from perfect).

Changes in cerebral blood flow and oxygen extraction during post-resuscitation syndrome[☆]

Virginie Lemiale^{a,1}, Olivier Huet^{a,d,e,f,1}, Bernard Vigué^{e,f},
Armelle Mathonnet^{a,d}, Christian Spaulding^{c,d}, Jean-Paul Mira^{a,d},
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Changes in cerebral blood flow following cardiac arrest

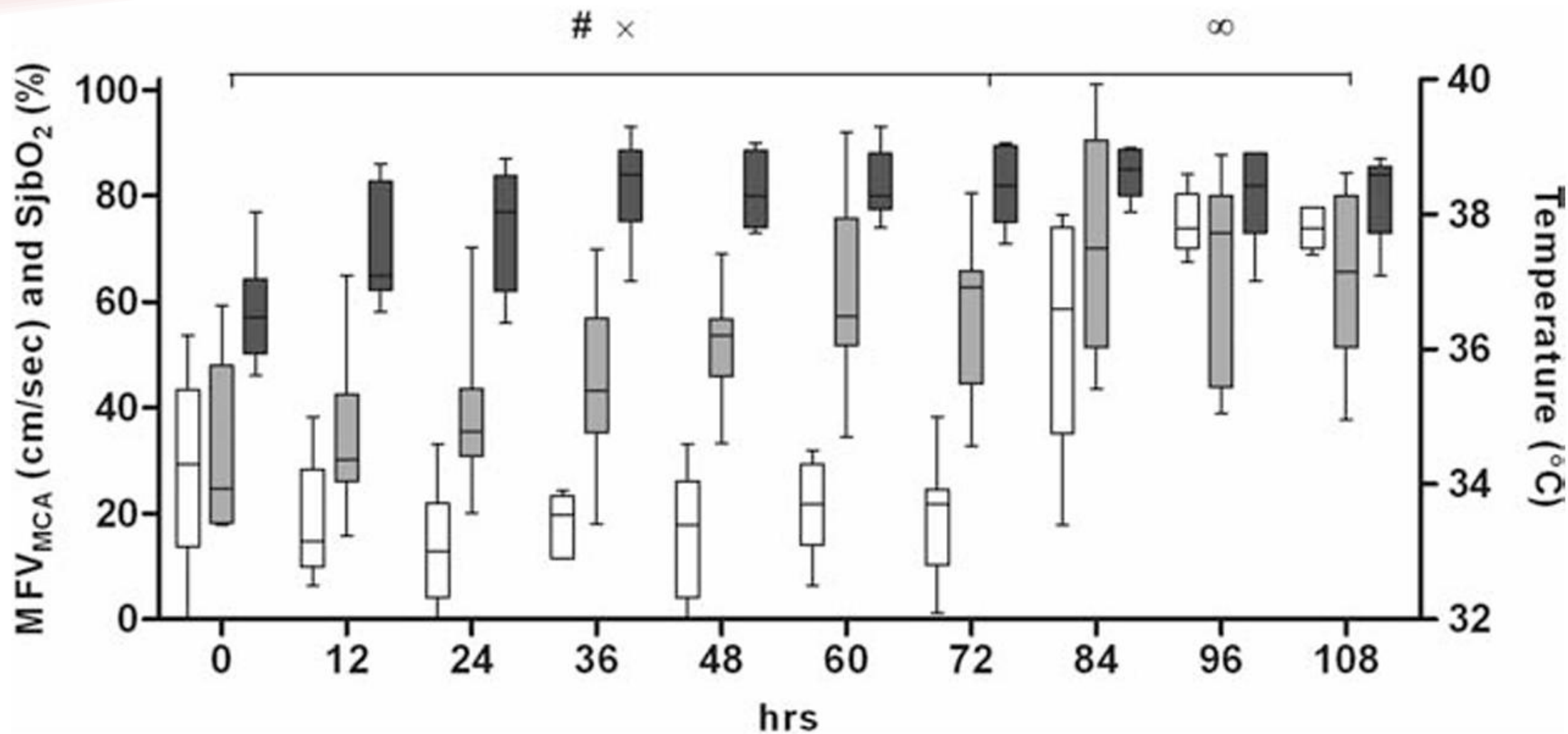
This is a single-centre observational study from Paris, with patients recruited in 2005. Consistent with international consensus practice at the time, survivors of CA were actively cooled to 32-34 degrees for 24hrs after ICU admission, followed by a period of passive rewarming. Mean arterial pressure was targeted between 75mmHg and 85mmHg. CBF was estimated using TCD, and cerebral oxygen extraction estimated using a retrograde jugular vein cannula. They measured PSV, DPV, time-averaged mean and PI. 18 patients were recruited – of whom 6 were still alive at day 28 (of the 12 patients who died, 9 or 10 died secondary to neurological injury – it is variously reported within the paper) – however TCD windows were not achievable in 2 of the 18 patients.

The authors found that mean and diastolic velocities were below the usual cut-offs at admission and for the first 24hrs, subsequently rising to normal levels (suggesting initial hypoperfusion followed by restoration of flow after the first day). Cerebral oxygen extraction was initially 'normal' despite inferred decreased CBF, with a subsequent fall in OER once CBF increased.

Whilst this study showed an initial hypoperfusion phase (which has also been described in other human and animal studies), in this small studies there was no difference in early flow velocities in between survivors and non-survivors.

Effects of prolonged mild hypothermia on cerebral blood flow after cardiac arrest

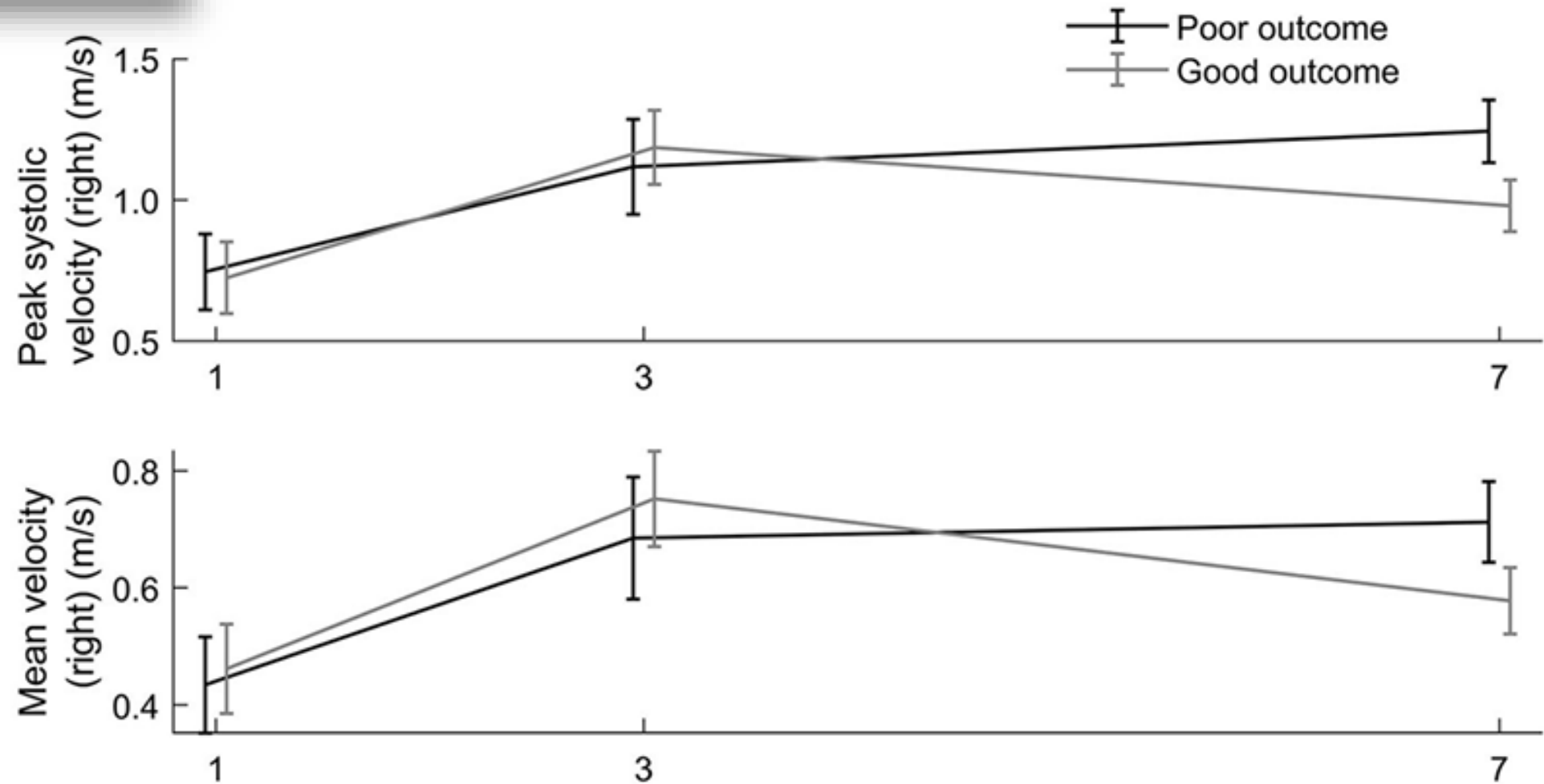
Laurens L. A. Bisschops, MD; Johannes G. van der Hoeven, MD, PhD; Cornelia W. E. Hoedemaekers, MD, PhD



This prospective observational study is from the Netherlands. Their standard of care was for 72 hours of 'prolonged' mild hypothermia following ICU admission for CA survivors. They recruited 10 patients and followed them for 4.5 days. This graph shows temperature in white bars (showing maintenance of temperature <34 degrees for the first 72 hours). The light grey boxes represent mean MCA velocity, and as with other studies, there is an initial phase where mean velocities are low, followed by a 'normalisation' after the first day. This rise in velocity occurs before the mild hypothermia treatment is discontinued. The graph also shows jugular oxygen saturations (dark grey boxes), and shows that this is low at presentation, and then normalises in concert with normalisation of CBF. 6 of 10 patients died in the ICU.

Transcranial Doppler during the first week after cardiac arrest and association with 6-month outcomes

Antje Reichenbach¹, Lars Alteheld², Julia Henriksen²,
Espen Rostrup Nakstad^{3,4}, Geir Øystein Andersen⁵, Kjetil Sunde^{6,7},
Jūratė Šaltytė Benth^{8,9} and Christofer Lundqvist^{1,8,9*}



This is a Norwegian study and looks at a subset of patients recruited into a larger study called NORCAST (which looked at factors that predicted poor neurological outcome after CA). 139 patients in that study had regular TCD assessment (they had hoped to perform this test on the total cohort – 259 patients – but data was missing from roughly half, principally due to technical reasons such as ‘early death’ and ‘early transfer to other hospitals’), of whom 81 (56%) were alive and CP 1-2 at 6 months. As in previous studies mean velocities rose from initial measurements over the first few days, although it is worth noting that not all patients were measured at all time points, indeed only 52 patients (37%) contributed a PSV and meanV value on day 1, only 44 patients (32%) contributed on day 2-3 and only 109 patients (78%) contributed on day 5-7. They found no difference between survivors and non-survivors initially, but found significant separation after 7 days (with non-survivors having both higher peak and mean velocities). If this finding is genuine and reproducible it would need to be ascertained if the elevated CBF observed at day 5-7 contributed to the poor outcome, or rather was a consequence of a greater degree of injury.

Each of these studies found that in patients resuscitated following CA, there is a global decrease in CBF (as implied by decreased flow velocities in the MCA, as assessed by Doppler US). Whilst the numbers are small there does not appear to be a signal to suggest that lower blood velocity is associated with worse neurological outcome. Therefore, based on the data provided here, it is difficult to conclude that early restoration of ‘normal’ CBF should be a therapeutic goal.

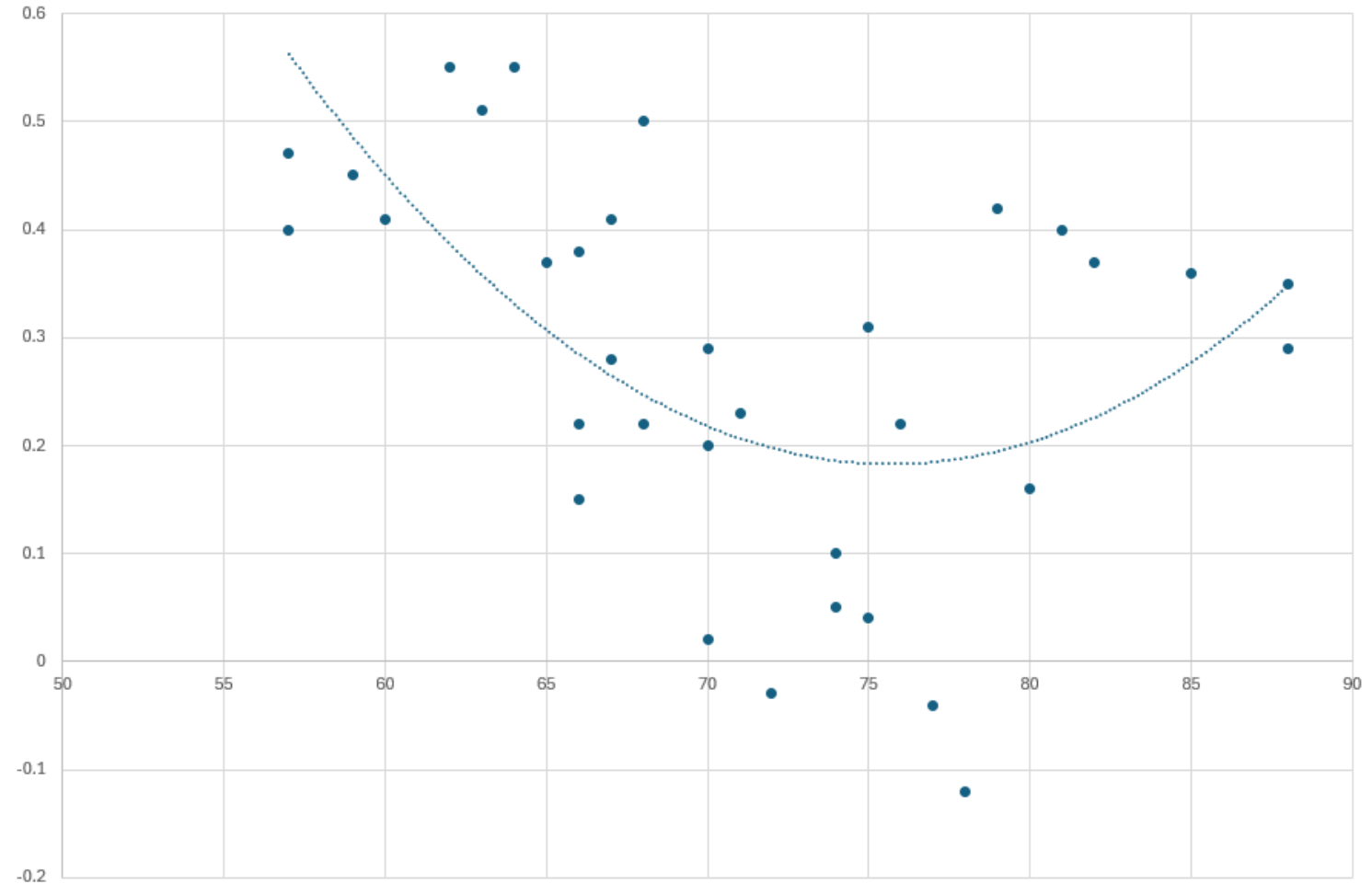
RESEARCH

Open Access

Association of deranged cerebrovascular reactivity with brain injury following cardiac arrest: a post-hoc analysis of the COMACARE trial

Johanna Laurikkala^{1*}, Anders Aneman^{2,3,4}, Alexander Peng², Matti Reinikainen⁵, Paul Pham⁶, Pekka Jakkula¹, Johanna Hästbacka¹, Erika Wilkman¹, Pekka Loisa⁷, Jussi Toppila⁸, Thomas Birkelund⁹, Kaj Blennow^{10,11}, Henrik Zetterberg^{10,11,12,13} and Markus B. Skrifvars¹⁴

- Automated software can track the relationship between MAP and brain StO₂ (assessed with NIRS) in real time.
- This is an example graph plotting MAP (x-axis) against TO_x (the coefficient of MAP and StO₂, y-axis).
- The ‘optimal’ MAP is defined as the nadir of the 2nd order polynomial trendline, here ~75mmHg.
- The target range is defined by where the trendline intersects with a TO_x value of 0.3, here ~65-86mmHg (range 21mmHg).



The COMACARE study (Jakkula, ICM, 2018) was a multi-centre RCT (6 ICUs in Finland and 1 in Denmark) which simultaneously randomised patients to one of two therapies in each of three arms: low-normal or high-normal $p\text{CO}_2$; normoxia or mild hyperoxia; MAP 65-75mmHg or MAP 80-100mmHg. When analysing the 120 patients based on MAP target, there was no difference in the primary outcome, NSE concentration at 48hrs post-CA. In addition, there was no significant difference in the secondary outcome of good neurological outcome (alive and CPC 1-2) at 6 months (seen in 62% vs. 68% of patients, $p=0.44$).

The study involved continuous monitoring of cerebral StO_2 with NIRS (Near Infra-Red Spectroscopy). The authors assessed (protocol published prior to study commencement) how fluctuations in MAP translated into changes in NIRS readings (which they refer to as Tissue Oximetry index, or TOx). The mechanism to estimate TOx takes a little explaining. Firstly, automated software records multiple 10-second averages of the (average right and left) NIRS value and MAP value. Secondly, these are correlated over moving 10-minute windows and the correlation coefficient is calculated. A coefficient >0 suggests that a rise in MAP results in a rise in NIRS, suggesting impaired cerebrovascular reactivity (of which autoregulation is one component). The closer the coefficient is to +1, the more NIRS is dependent upon MAP. The closer to 0 the more unrelated the values are, and a value of -1 means that any fall in NIRS can be entirely explained by a rise in MAP. This correlation coefficient is termed TOx. Thirdly the MAP and TOx values associated with that MAP are plotted on a scatter graph and a 2nd order polynomial trendline is fitted. The nadir of this U-shaped trendline is considered the 'optimal' MAP, as it is the MAP at which a rise in NIRS can be least attributed to a rise in MAP. The U-shaped trendline will cross the TOx value of 0.3 twice (once on either side of the nadir), and where the trendline crosses this value, the associated MAP values are considered the lower and upper bounds of the target MAP range.

RESEARCH

Open Access

Association of deranged cerebrovascular reactivity with brain injury following cardiac arrest: a post-hoc analysis of the COMACARE trial

Johanna Laurikkala^{1*}, Anders Aneman^{2,3,4}, Alexander Peng², Matti Reinikainen⁵, Paul Pham⁶, Pekka Jakkula¹, Johanna Hästbacka¹, Erika Wilkman¹, Pekka Loisa⁷, Jussi Toppila⁸, Thomas Birkelund⁹, Kaj Blennow^{10,11}, Henrik Zetterberg^{10,11,12,13} and Markus B. Skrifvars¹⁴

- 76 of 108 patients (70%) had an average TOx value >0, described as having ‘impaired cerebrovascular reactivity’.
- Patients with impaired CVR were older and more likely to have a diagnosis of hypertension.
- Patients with a poor outcome at 6-months had significantly higher average TOx values.
- There was a non-significant trend towards worse outcomes in patients with impaired CVR (34% vs. 28%).
- ‘Optimal’ MAP varied highly in patients with good and bad outcomes.
- There was no significant difference in time spent within, below or above the optimal MAP range.

The authors state that impaired cerebrovascular reactivity was seen in 76 of 108 analysed patients (70%). These were patients who exhibited an average TOx value >0 (in the example graph provided on the previous slide, the average TOx was 0.28). The remaining 32 patients were described as having intact CVR (average TOx ≤ 0).

Impaired CVR was seen more commonly in older patients (median age 61-years vs. 55-years) and patients with a history of systemic hypertension (58% vs. 31%). Amongst patients labelled as having impaired CVR, there was a non-significant trend towards worse outcomes at 6-months (34% vs. 28%). The average TOx value (over the 48-hour period of assessment) was higher in patients with a poor outcome ($p=0.004$). The data provided (including that in the supplement) does not allow for an assessment of whether a cut-off of value of TOx could be proposed that might predict a poor outcome (the impression is that it couldn't).

The 'optimal' MAP as estimated by this method was highly variable (both in those with a good and bad outcome) and ranged from being within the 55-65mmHg window to within the 105-115mmHg window. The authors looked to see if patients with different outcomes were more or less likely to have spent more time within their individualised target MAP range (or below the lower bound, or above the upper bound) and did not find a significant difference.

Transcranial Doppler goal-directed therapy after cardiac arrest (GOODYEAR): a feasibility study

*Juliette Meunier^a, Nicolas Engrand^b, Patrick Saulnier^c, Nicolas Deye^{d,e,g},
Mickaël Landais^a, Alain Cariou^{f,g}, Christophe Guitton^a, Nicolas Chudeau^{a,g,*}*

- 172 patients admitted to ICU following CA were screened, during a ~3-year window.
- TCDs were attempted in 28 patients, and views achieved in 20 patients (72%).
- 3 patients had an ‘abnormal’ Doppler pattern (elevated PI and low dFV or mFV).
- MAP challenge was attempted in 2 of these. Noradrenaline was used to raise MAP to >100mmHg resulting in a rise in estimated ICP without a normalisation of the Doppler pattern.
- In this study TCDs were rarely performed, frequently non-diagnostic and interventions may have resulted in harm, without any signal for benefit.

This is a single-centre study from Le Mans (France). Patients had jugular vein lines inserted for measuring cerebral OER, and TCD was performed as soon as possible after stabilisation (T_1), and then at 6, 12 and 24 hours. Patients were labelled as having 'abnormal cerebral Doppler ultrasound' if they had $PI > 1.4$ and at least one of mean velocity (mFV) $< 0.3\text{m/s}$ or diastolic velocity (dFV) $< 0.2\text{m/s}$ (the patients was labelled as abnormal if measurements made on either side of the head met these criteria). Doppler was used to estimate CPP and ICP, using the following formula... $eCPP = MAP \times dFV/mFV + 14$... $eICP = MAP - eCPP$. Cerebrovascular resistance was estimated as MAP/mFV , with mFV used as a surrogate for blood flow (interestingly MAP and not eCPP was used as the pressure component of the resistance equation).

In patients in whom an abnormal pattern was identified at baseline (T_1), a noradrenaline intravenous infusion was up-titrated to raise the MAP by 10mmHg, and then the TCD was repeated 20 minutes after reaching the new MAP. If the Doppler profile had 'normalized' no further MAP rise was performed, but if it remained abnormal there was a further rise in the MAP by 10mmHg and another reassessment was made. This cycle continued until the MAP of 110-120mmHg was reached. The lowest MAP at which the Doppler profile normalized was the target MAP for the first 24hrs. Patients who never responded (i.e. a 'normal' profile was never achieved) were managed with a MAP $> 65\text{mmHg}$ (in line with guidelines). Whilst TCDs were performed at later time-points, there was no associated MAP challenge.

Initial (at T_1) static autoregulation was calculated by dividing the change in CVR (from initial to final TCD measurement) by the change in MAP. As no MAP challenge was performed in patients with an initial normal Doppler pattern, static autoregulation could not be assessed in these patients.

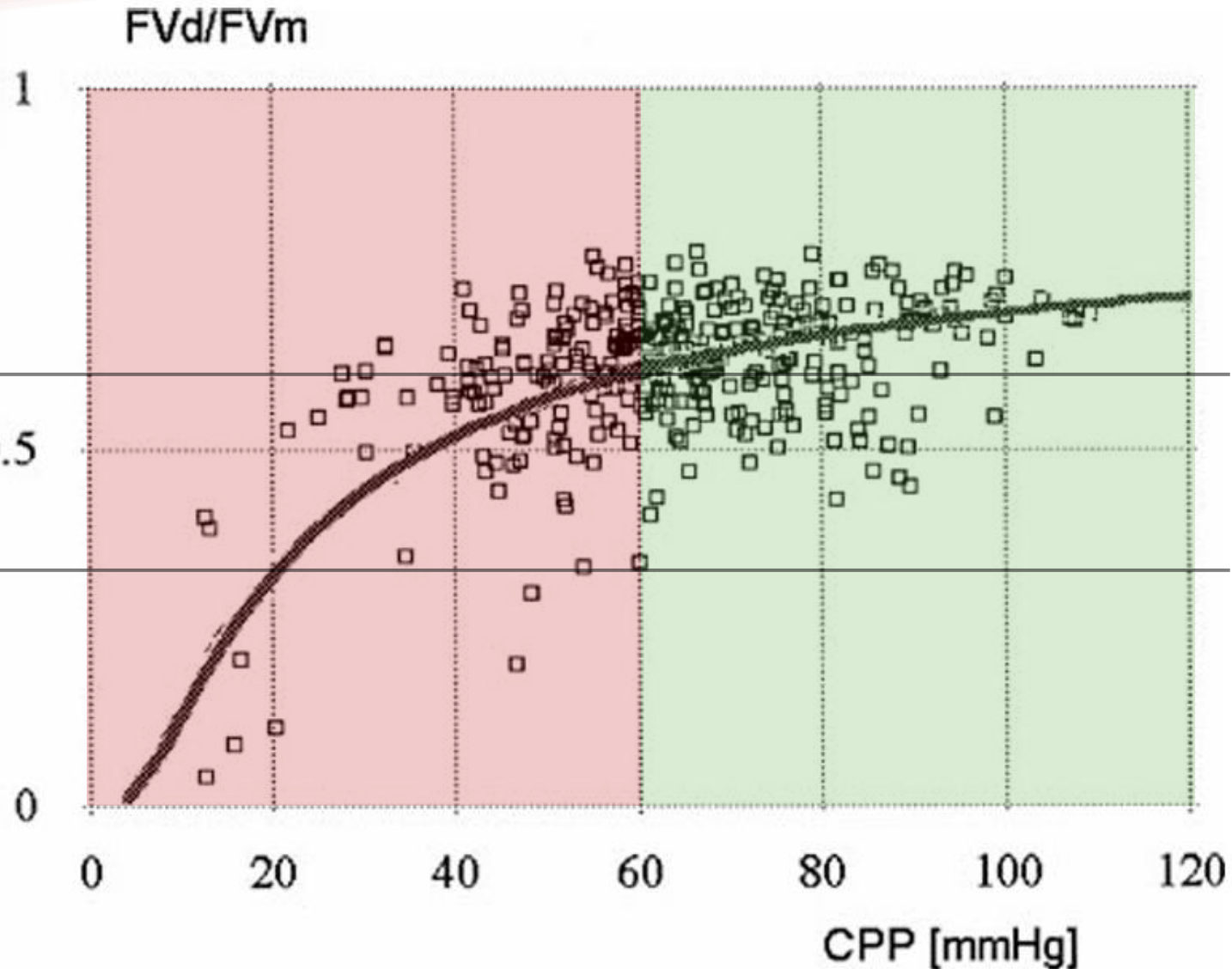
Over a 3-year period 172 patients were screened, but 52 were ineligible due to haemodynamic instability. After other exclusion criteria were considered this left 101 patients. However, TCD was only attempted in 28, and views were inadequate in 8 of these (28%). In the 20 patients assessed, initial TCD was performed at a median of 8.4 hours after ROSC (IQR 5.5-18.8 hours). Only 3 patients (15%) had an abnormal profile. Of the 3 patients with an abnormal profile a MAP challenge was only performed in 2 (as the third was haemodynamically unstable). In the first of these two patients MAP was raised from 75mmHg to 117mmHg, with an associated rise in eICP of +24mmHg, and in the second MAP rose from 73mmHg to 101mmHg, with an associated rise in eICP of +9mmHg. When MAP was raised this failed to result in a normalisation of Doppler profile.

Cerebral perfusion pressure in head-injured patients: a noninvasive assessment using transcranial Doppler ultrasonography

MAREK CZOSNYKA, Ph.D., BASIL F. MATTA, M.B., F.R.C.A., PIOTR SMIELEWSKI, Ph.D.,
PETER J. KIRKPATRICK, M.D., F.R.C.S., AND JOHN D. PICKARD, M.Chir., F.R.C.S.

PI 1.2

PI 2.0



Trans-Cranial Doppler for the estimation of Intra-Cranial Pressure

This is a single centre study from Addenbrooke's (Cambridge). The study included 96 patients who had suffered severe TBI (not decompressed) who were sedated and muscle-relaxed on ICU, with invasive ICP monitoring. TCDs were performed daily (total of 421 measurements). They compared the ratio of EDV to mean velocity (or perhaps TAPV, cannot be certain from the text). This ratio is inversely proportional to pulsatility index, indeed if the calculated mean is used (rather than TAPV), then PI can be calculated from FVd/FVm using the formula: $PI = 3 \times (1 - FVd/FVm)$. So $FVd/FVm > 0.6$ equates to $PI < 1.2$ and $FVd/FVm < 0.33$ equates to $PI > 2.0$. If TAPV is used (as opposed to a calculated mean) then the formula is approximate (rather than absolute).

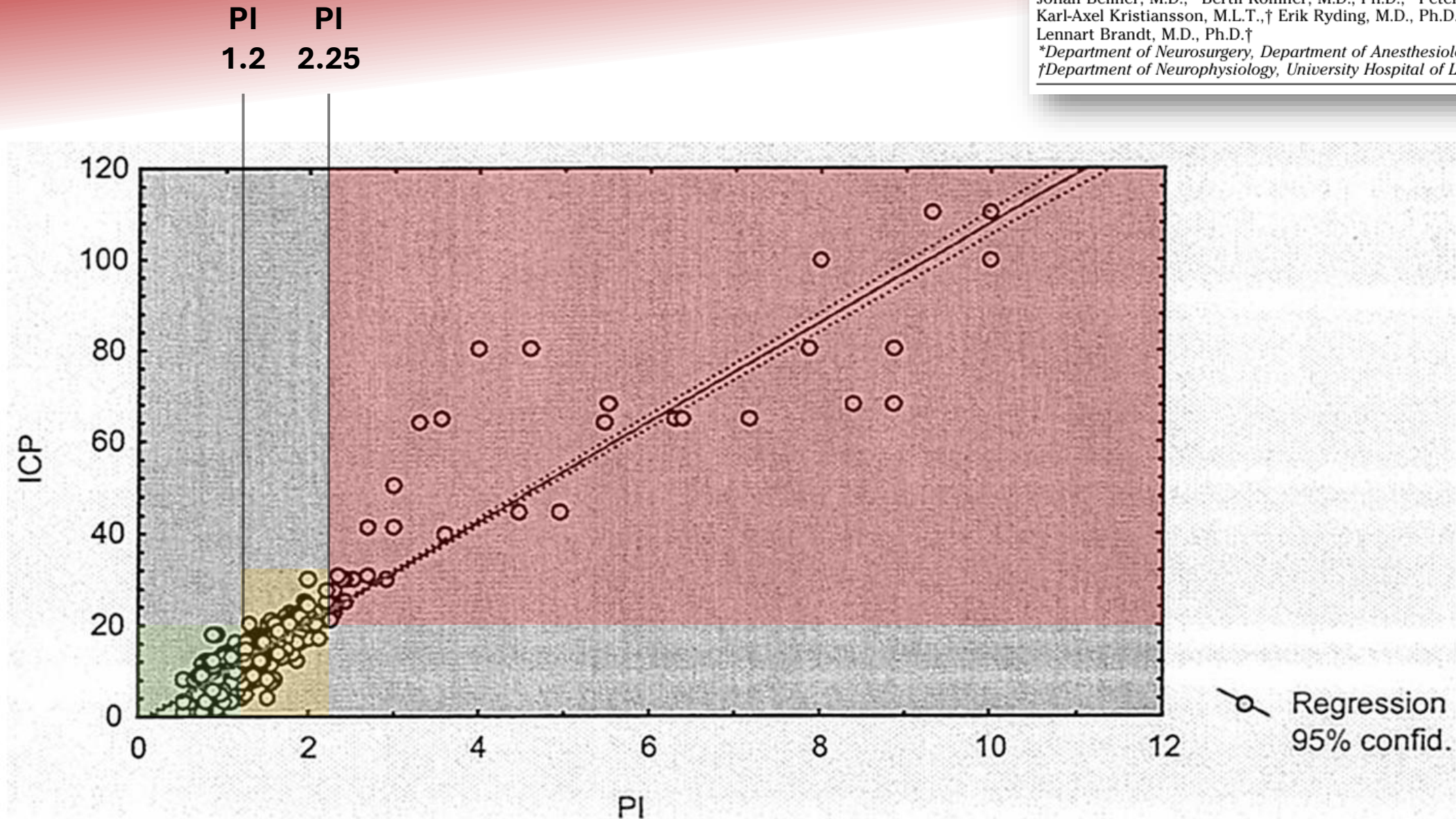
The correlation was reasonable ($r=0.65$). They then used this relationship to propose a formula that could be used to estimate CPP (eCPP) from MAP and FVd/FVm: $eCPP = 7.72 + 1.14 \times MAP \times FVd/FVm$. When this equation was applied to their cohort, there was a 94% PPV of the true CPP being below $<60\text{mmHg}$ when eCPP was $<60\text{mmHg}$. However, the NPV was only 38% (i.e. an eCPP $<60\text{mmHg}$ means true CPP is very likely to be $<60\text{mmHg}$, however when eCPP was $>60\text{mmHg}$, most patients still had a CPP $<60\text{mmHg}$), so charitably this could be considered a rule in test and certainly not a rule out test. They then proposed that the equation could be simplified: simplified eCPP = $MAP \times FVd/FVm + 14$. When this simplified equation the measured CPP was within 10mmHg (+/-) of the eCPP on 71% of occasions. Given CPP is a function of ICP and MAP, this equation can then be rearranged to produce the equation: $eICP = MAP \times (1 - FVd/FVm) - 14$.

Given, even when using the best possible equations, eCPP point estimates are out by $> +/- 10\text{mmHg}$ in 29% of cases (and therefore eICP will also be out by $> +/- 10\text{mmHg}$ in 29% of cases) I would personally be very wary of using TCD (essentially PI) to produce a point estimate of ICP using this technique.

TRANSCRANIAL DOPPLER SONOGRAPHY PULSATILITY INDEX (PI) REFLECTS INTRACRANIAL PRESSURE (ICP)

Johan Bellner, M.D.,* Bertil Romner, M.D., Ph.D.,* Peter Reinstrup, M.D., Ph.D.,*
Karl-Axel Kristiansson, M.L.T.,† Erik Ryding, M.D., Ph.D.,† and
Lennart Brandt, M.D., Ph.D.†

*Department of Neurosurgery, Department of Anesthesiology & Intensive Care and
†Department of Neurophysiology, University Hospital of Lund, Lund, Sweden

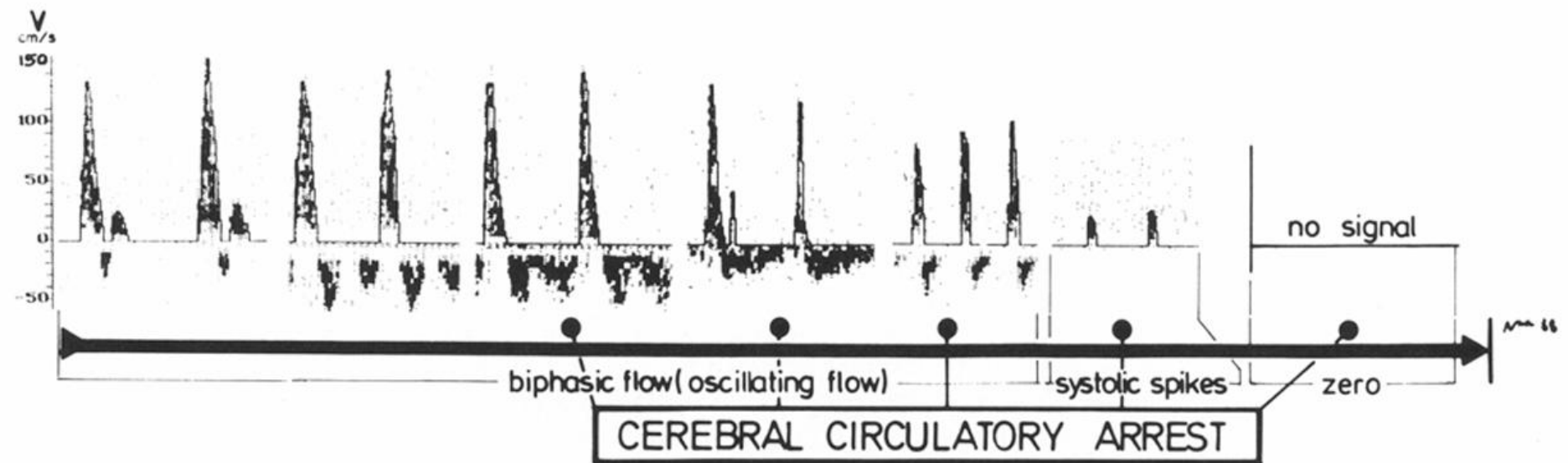
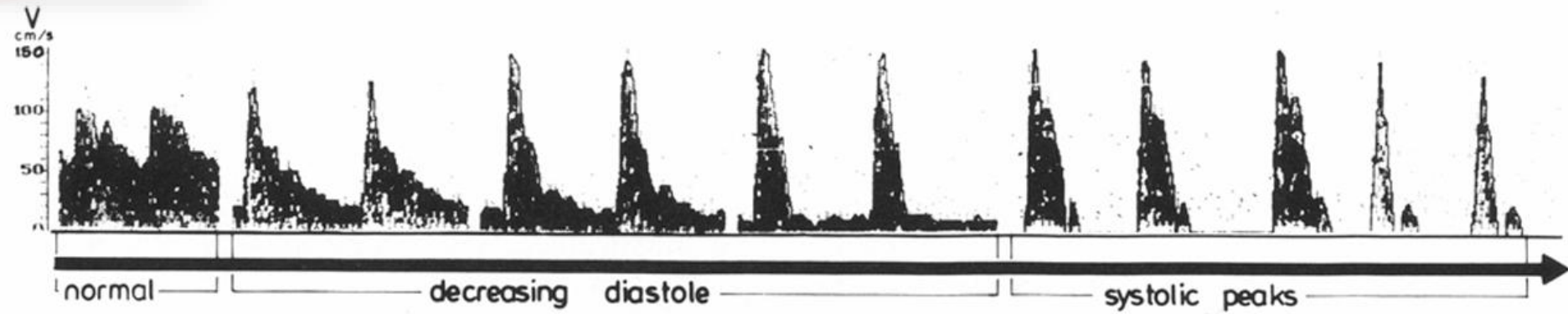


This is a prospective single centre study from Lund (Sweden). The study recruited 81 patients with a variety of different pathologies (57% aneurysmal SAH, 26% severe TBI, 9% spontaneous ICH, 9% other), in whom 658 PI measurements were made. There was a modest correlation between PI and CPP ($r=-0.493$) and an excellent correlation with ICP ($r=0.938$). The correlation remained strong when considering only patients with low flow velocities (mean $<50\text{cm/s}$) or only patients with high velocities ($>120\text{cm/s}$). When looking at figure 2 from this study, we can see that all patients with $\text{PI} < 1.2$ had a simultaneous ICP measurement $\leq 20\text{mmHg}$, patients with a PI of (approximately) 1.2-2.25 had ICPs within the range 0-30mmHg and patients with a $\text{PI} > 2.25$ had an $\text{ICP} \geq 20\text{mmHg}$. The authors used the regression line to allow TCD estimated ICP (eICP) to be extrapolated from the PI, using the formula: $\text{eICP} = 11.5 \times \text{PI} - 2.23$. Using this formula a PI of 1.93 would yield an eICP of 20mmHg.

Note: The B-ICONIC paper was a consensus statement produced via a Delphi process, which made recommendations on the use of non-invasive techniques to estimate ICP. Early in their results section they state, 'Clear evidence is available regarding the fact that none of the available nICP tools is, at present, accurate enough to substitute invasive tools...'. With respect to the use of TCD they state 'For TCCD use, we suggest considering a threshold of PI of 1.3 in conjunction with a $\text{FVd} < 20\text{cm/sec}$ as a threshold for considering low CBF potentially associated to high ICP, or for excluding it' (strong recommendation based on low level of evidence). They continue, 'We recommend that to raise/exclude the suspect of intracranial hypertension, a change from basal level of PI of at least 0.5 should be considered as a sign of CBF modification potentially related to ICP shift' (strong recommendation based on expert opinion, no evidence available).

Transcranial Doppler study of intracranial circulatory arrest

WERNER HASSLER, M.D., HELMUTH STEINMETZ, M.D., AND JÜRGEN PIRSCHEL, M.D.



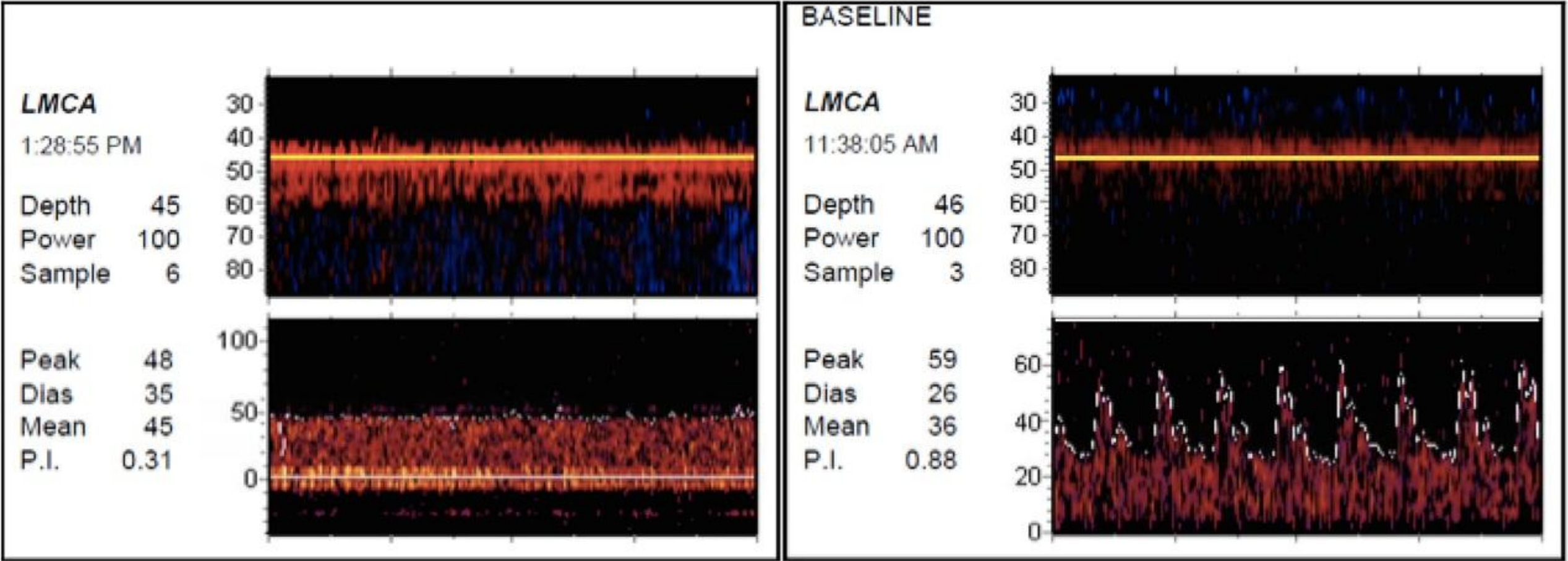
Trans-Cranial Doppler as a sign of circulatory arrest

When ICP becomes very elevated CPP can fall to the point of cerebral circulatory arrest. Hassler et al. (Journal of Neurosurgery, 1989) published a series of 65 patients who died due to intracranial hypertension (of various causes). All patients were confirmed to have died by neurological criteria, and all underwent EEG demonstrating an isoelectric pattern for 30 minutes. Following confirmation of death trans-femoral four-vessel cerebral angiography was performed, and the findings were compared with immediately pre-angiography TCD pattern (patients were divided between those showing 'biphasic flow', those with 'systolic spikes' and those with 'zero flow'). Patients were only labelled as having zero flow if there had been confirmed flow demonstrated on TCD previously (i.e. flow had been seen to cease, as there is a risk of erroneously labelling a patient with poor windows as having zero flow).

The different patterns correlated with anatomical level of circulatory arrest. More advanced TCD patterns correlated with more proximal flow cessation. In patients with biphasic flow the most frequently observed patterns (on 81% of occasions) were termination of flow at the anterior clinoid process (posterior projection of the sphenoid bone) or stasis filling (with contrast terminating in the subarachnoid arteries, and no subsequent venous enhancement), with the remaining patients exhibiting more proximal flow cessation. In patients with zero flow on TCD, flow always ceased prior to the anterior clinoid process, and usually (on 89% of occasions) in the extra-cranial C1 segment of the ICA.

Transcranial Doppler Changes in Patients Treated with Extracorporeal Membrane Oxygenation

Tapan Kavi, MD, Megan Esch, MD, Brenda Rinsky, RVT, RDMS, Axel Rosengart, MD, PhD, Shouri Lahiri, MD, and Patrick D. Lyden, MD



Trans-Cranial Doppler patterns in patients receiving V-A ECMO

So far, we have only considered TCD patterns in patients whose circulation is entirely driven by the heart. As V-A ECMO will result in either exclusively non-pulsatile flow (when the heart is not ejecting), or a mix of pulsatile and non-pulsatile flow (when the heart is ejecting, which is expected to be the case on the vast majority of occasions), then it should be expected that PI will be influenced not only by cerebral resistance, but also cardiac function and ECMO settings.

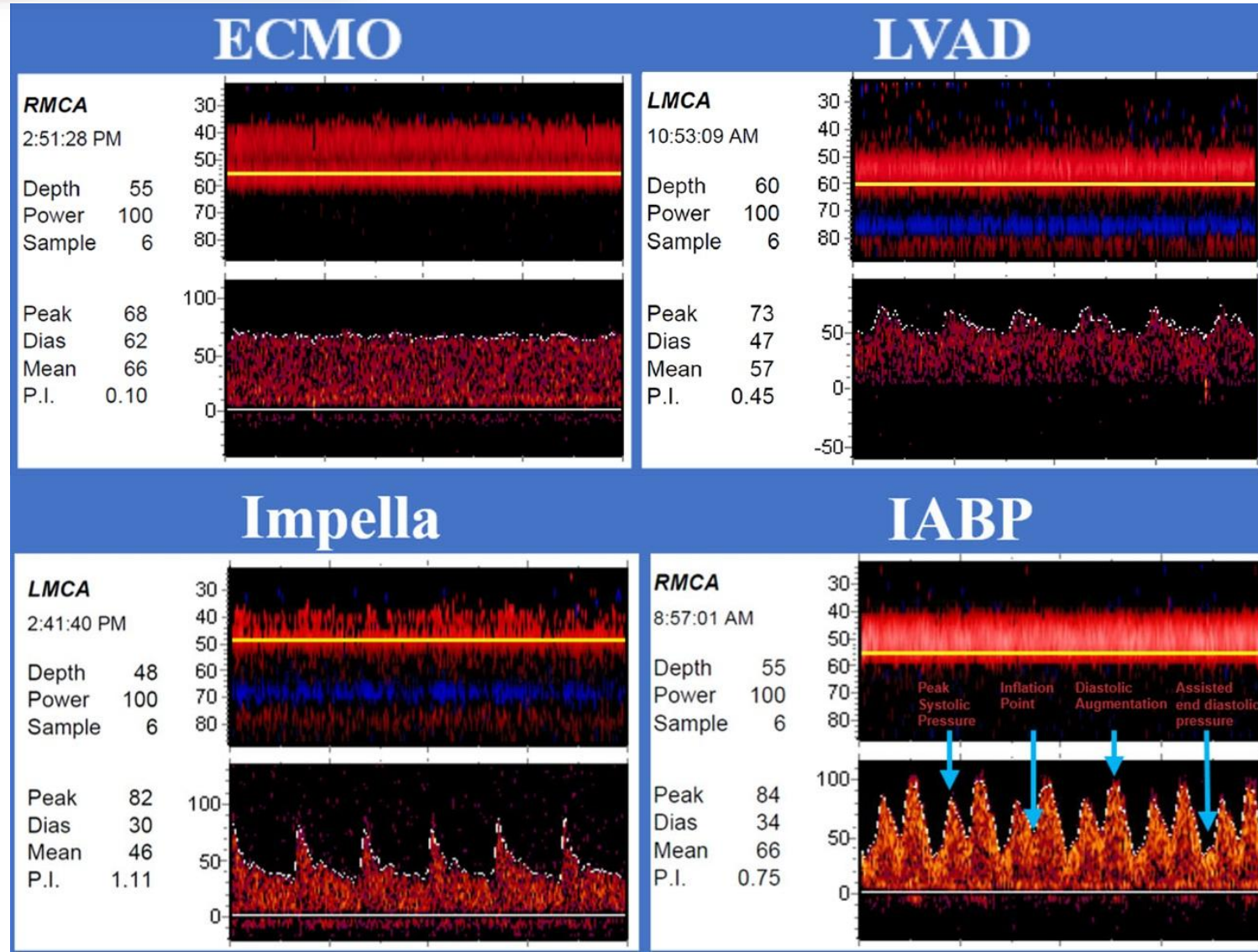
This study (Kavi, Journal of Stroke and Cardiovascular Diseases, 2016) looked at 8 patients receiving V-A ECMO. When looking at the first set of TCDs for each of the 8 patients, the mean (of left and right) PIs ranged from 0cm/s (non-pulsatile) to 0.63, with an average (of the 8 patients) of 0.32. PI was reported to correlate with EF. Whilst the paper does not quote the strength of the correlation, individual patient data is provided. If we look at the first set of TCDs for each patient and substitute a point estimate of LVEF 5% when it is reported as <10%, then $r^2 = 0.59$.

The figure displayed above shows LMCA TCD from the same patient, whilst on V-A ECMO with LVEF 10% (reported to show a PI of 0.31, although the trace looks essentially flat to my eye) and following placement of a total artificial heart (with pulsatile flow).

Assessing Cerebrovascular Hemodynamics Using Transcranial Doppler in Patients with Mechanical Circulatory Support Devices

Kara R. Melmed , Konrad H. Schlick, Brenda Rinsky, Oana M. Dumitrascu, Oksana Volod, Mani Nezhad, Matthew M. Padrick, Carmelita Runyan, Francisco A. Arabia, Jaime D. Moriguchi, Patrick D. Lyden, Shlee S Song

- Patients supported with V-A ECMO frequently have TCD traces without clear systolic peaks, even when the heart is ejecting.
- This study found the mean PI amongst 27 patients supported with V-A ECMO was 0.43 (NR 0.81-0.97), with a large SD.
- The authors do not describe the relationship between cardiac function, device settings and PI.



This study (Melmed, Journal of Neuroimaging, 2020) the authors performed TCDs in patients supported by a range of MCS devices. 86 patients were studied, of whom 28 were receiving V-A ECMO (TCDs were performed on 11% of the 257 patients who received V-A ECMO).

ORIGINAL WORK

Characterization of Cerebral Hemodynamics with TCD in Patients Undergoing VA-ECMO and VV-ECMO: a Prospective Observational Study

Giorgio Caturegli^{1*}, Lucy Q. Zhang¹, Yunis Mayasi¹, Aaron M. Gusdon¹, Bahattin Ergin¹, Vladimir Ponomarev¹, Bo Soo Kim², Steven Keller², Romergryko G. Geocadin¹, Glenn J. R. Whitman², Sung-Min Cho¹ and Wendy Ziai¹ on behalf of HERALD (Hopkins Exploration, Research, and Advancement in Life support Devices) Investigators



MFV	Normal, mean $\pm$ SD (cm/s)	VA-ECMO ($n = 95$ studies), n (%) or median (IQR) (cm/s)	
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Right			
MCA M1	60.1 $\pm$ 12.1	84 (88.4%)	52 (40–71)
Left			
MCA M1	60.1 $\pm$ 12.1	82 (86.3%)	51 (37–70)

PI	VA-ECMO ($n = 95$ studies), n (%)	VA-ECMO % abnormal (≥ 1.2), n (%)	PI, median (IQR)
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Right			
MCA M1	47 (49.5)	22 (46.8)	1.1 (1.0–1.6)
Left			
MCA M1	46 (48.4)	25 (54.5)	1.2 (1.0–1.6)

- There is a trend to low mean velocities in patients on V-A ECMO (~25% of patients below the lower limit of the reference interval).
- In just over half of patients, the TCD trace was considered non-pulsatile.
- Patients with a non-pulsatile trace had lower pulse pressures (18mmHg v 46mmHg), suggesting cardiac function and device settings influence MCA pulsatility.
- When PI was measured, it was frequently high.
- ICH confirmed in 15% of patients without pulsatility.

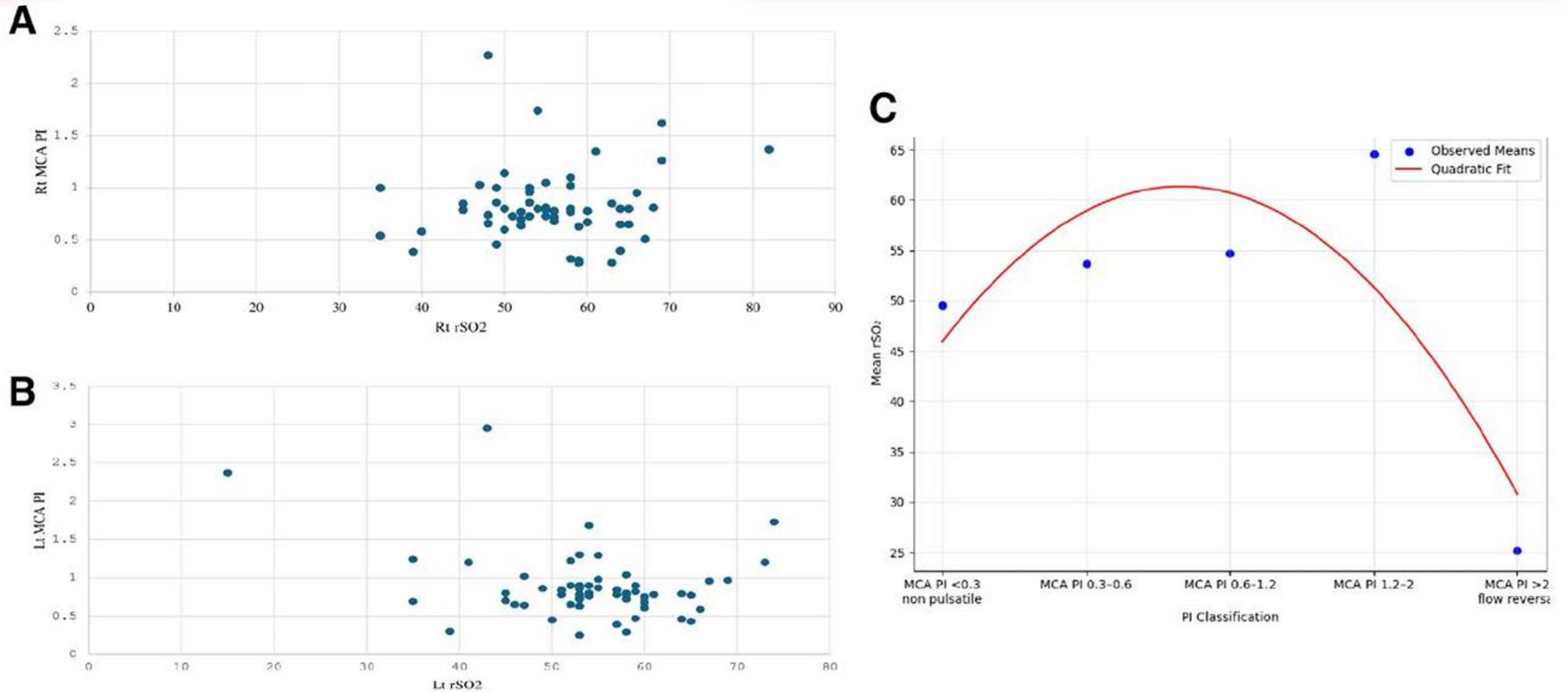
This is a large single-centre (Caturegli, Neurocritical Care, 2023) from John Hopkins University Hospital, Baltimore (USA). They introduced a neuromonitoring protocol for patients receiving V-V and V-A ECMO in 2017, and used this protocol for all patients other than those who died early or when logistical reasons prevented it be applied (mostly during the COVID-19 pandemic). The protocol was for all patients on ECMO to have TCDs performed (using a 'blind' Doppler system) on D1, D3-5 and D7-10, performed by a specialist vascular sonographer, and involving bilateral ICAs (C1), MCAs (M1), ACAs (A1), vertebral arteries and the basilar artery. Additional TCDs were allowed if clinically indicated. The authors compared mean (from right and left M1 segments of the MCA) mean velocity (likely TAPV) and PI in patients receiving ECMO against reference intervals derived from a cohort of healthy volunteers (Tegeler, Journal of Neuroimaging, 2013).

Over a 4-year period 215 patients received ECMO, of whom 135 received at least one TCD study. 95 of these patients were receiving V-A ECMO (roughly 50/50 split between cV-A and pV-A, with 30% having IABP in situ, and a small number having an LVAD, presumably a micro-axial flow catheter), and 81 (85%) of these patients had windows which allowed assessment of mean velocity.

In patients receiving V-A ECMO, the average mean velocity was lower than in healthy controls. If we use 2 standard deviations to calculate a lower reference interval in healthy volunteers used in this study, then this comes out at 36cm/s, and from the IQRs quoted for patients on V-A ECMO, we can see that ~25% of patients had 'low' mean velocity. Despite achieving windows from which mean MCA velocities could be measured in most patients, the PI is reported in less than half of patients receiving V-A ECMO (in most patients the trace was considered non-pulsatile). By contrast PI could almost always be measured in patients receiving V-V ECMO. Pulse pressure at time of TCD study was highly correlated with ability/inability to measure the PI (mean PP in patients with measurable PI was 46mmHg (IQR 34-60mmHg), and only 18mmHg (IQR 6-44mmHg) in patients without a measurable PI). 14.7% of patients with a non-pulsatile TCD trace had confirmed intra-parenchymal hemorrhage.

Cerebro-Cardiovascular Coupling During Extracorporeal Membrane Oxygenation Using Cerebral Oxygenation, Doppler Flow, and Echocardiography

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This is a single-centre study (Roushdy, ASAIO, 2026) from Cairo University Hospital, Egypt. 25 patients receiving V-A ECMO were screened, and 17 had temporal windows (68%) and were included in the study. The majority of patients (11, 65%) were suffering from aluminum phosphide poisoning (pesticide). Serial assessments were made in these patients, with a total of 64 assessments made. MCA flow was usually pulsatile (55, 86%). Regional cerebral oxygen saturations were measured with NIRS (near infra-red spectroscopy). Both left and right MCAs were assessed. Interestingly there was a significant difference between right and left PSV and mean velocity, which were typically higher on the left (on average ~5cm/s and ~4cm/s respectively). There was no trend towards either hemisphere having higher rSO_2 on NIRS.

The authors compared the MCA PI with the rSO_2 . The correlation between PI and rSO_2 was poor ($r=0.1$ on the right, and $r=-0.29$ on the left). The authors report that 'nonlinear correlation analysis ... revealed a clear pattern' (as shown in figure C) with optimal PI in the range 0.6-1.2. I am dubious about how informative this graph is, as the mean rSO_2 value when PI was in the range 1.2-2.0 is far from the line of best fit, and the low mean rSO_2 associated with $PI > 2.0$ is the mean of just 3 values, one of which is an extreme outlier.

Summary:

- CBF falls during the first 24hrs following CA, in both survivors and non-survivors. There is a simultaneous fall in cerebral oxygen consumption. It is yet to be demonstrated if CBF is a therapeutic target.
- CBFV via TCD can be measured in ~70-85% of patients.
- CBFV correlates with CBF and Δ CBFV correlates with Δ CBF, but the relationship is far too poor for point estimates.
- In patients not receiving ECMO, an elevated PI (especially >2.0) suggests raised ICP and low CPP.
- In patients not receiving ECMO, circulatory arrest is associated with abnormal flow patterns: biphasic flow; systolic spikes; no flow (when flow had previously been demonstrated).
- In case series, around half of patients receiving V-A ECMO have non=pulsatile MCA flow (due to cardiac failure, as evidenced by low LVEF and low pulse pressure).
- In the largest case series, when PI was present, it was elevated (>1.2) in approximately half of patients receiving V-A ECMO.

Having reviewed this literature, how will I incorporate TCD into the management of a patient receiving V-A ECMO as part of ECLS?

I will not routinely perform this investigation (and it is not routinely performed at our centre). I suspect it is most useful when I have a patient who is ejecting reasonably well (so should have pulsatile flow in their MCA) in whom I am concerned about the possibility of a significant intracranial event and am weighing up the risk/benefit of a transfer to the CT scanner. In such a patient the absence of pulsatility (particularly if demonstrated previously) or an elevated PI (especially if ≥ 2.0) would raise my level of concern (especially if PI remains elevated despite therapeutic interventions). Conceivably this may play into the decision-making regarding CT transfer. I would not be reassured by any TCD trace and would not use TCDs in place of CT.