CEREBRAL AUTOREGULATION IN ADULTS UNDERGOING SEVOFLURANE ANESTHESIA: A PROSPECTIVE COHORT STUDY OF TWO AGE GROUPS

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Background

Autoregulation of blood flow is a key feature of the human cerebral vasculature to assure adequate oxygenation and metabolism of the brain under changing physiological conditions. Impaired cerebral blood flow (CBF) autoregulation is associated with various pathological and pharmacological states, and may be a trigger for poor neurological outcome such as silent ischemia and/or postoperative cognitive decline, which is more common in elderly patients. Little is known about the effect of inhalational anesthetic agents and advanced age on CBF autoregulation.

Methods

We conducted a prospective observational multicenter study (Basel and Lausanne University Hospitals) to determine the effect of sevoflurane anesthesia on individual CBF autoregulation in two age groups. All patients underwent standardized sevoflurane anesthesia for a major surgical intervention. Recorded by transcranial Doppler ultrasonography, cerebral hemodynamic data were computed to provide an individual CBF autoregulation curve for each patient. CBF autoregulation indices, thresholds, and ranges were compared in young and elderly patient groups.

Results

One hundred thirty-three patients (49 patients (37%) aged 18-40 years and 84 patients (63%) aged ≥65 years) were included in the study. Intraoperative minimum alveolar concentrations of sevoflurane were 0.94 ± 0.09 in young and 0.81 ± 0.12 in older subjects. Overall, the index of CBF autoregulation was significantly higher in older patients (0.5 vs 0.41, $P = 0.011$), indicating a decreased autoregulatory capacity in the elderly. Effective cerebral autoregulation was found only in a very narrow blood pressure range of 13.8 ± 9.8 mm Hg in younger and 10.2 ± 8.6 mm Hg in older patients. The lower threshold of autoregulation was 66 ± 12 mm Hg and 73 ± 14 mm Hg in younger and older patients, respectively.

Table 1. Classification of CBF Autoregulation Curves

Lower threshold	Curves of either one or both hemispheres start above the Mx limit and then drop below or directly on the Mx limit.
Upper threshold	Curves of either one or both hemispheres start below or directly on the Mx limit and then rise above it.
Two thresholds	Curves of either one or both hemispheres start below the Mx limit and then drop below or directly on the Mx limit, before rising above it again.
Maintained CBF autoregulation	Curves of either one or both hemispheres permanently remain below or directly on the Mx limit.
Lack of CBF autoregulation	Curves of both hemispheres permanently remain above the Mx limit.
Hemispherical difference	The curve of one hemisphere shows a "lower threshold", a "higher threshold", "two thresholds", or "maintained CBF autoregulation", independently of the curve of the other hemisphere.
Not interpretable	• Both curves are missing. • Any curves not falling into one of the categories above. • Operating (data collection) time less than 60 min.

CBF indicates cerebral blood flow; Mx, index of cerebral blood flow autoregulation

Table 2. Categories of CBF Autoregulation Curves in Study Groups

	All patients (n = 133)	Group 1 (≤40 years) (n = 49)	Group 2 (≥65 years) (n = 84)
Type "Lower threshold", n (%)	11 (8)	5 (10)	6 (7)
Type "Upper threshold", n (%)	10 (8)	3 (6)	7 (8)
Type "Two thresholds", n (%)	6 (5)	2 (4)	4 (5)
Type "Maintained CBF autoregulation", n (%)	18 (14)	7 (14)	11 (13)
Type "Lack of CBF autoregulation", n (%)	16 (12)	3 (6)	13 (15)
Type "Hemispherical difference", n (%)	37 (28)	14 (29)	23 (27)
Type "Not interpretable", n (%)	35 (26)	15 (31)	20 (24)
Both CBF curves missing, n (%)	6 (5)	0	6 (7)
CBF curves not categorical, n (%)	23 (17)	10 (20)	13 (15)
Operating time <60 min, n (%)	6 (5)	5 (10)	1 (1)

Data are presented as n (% within group). Data from study participants in the category "not interpretable" was excluded from further analysis. CBF indicates cerebral blood flow.

Table 3. Demographic and Intraoperative Data

	All patients	Group 1 (≤40 years)	Group 2 (≥65 years)	P
n (%)	98	34 (35)	64 (65)	
Patient characteristics				
Age (y)	58	31 ± 6	73 ± 7	
Male (n, %)	46 (47)	23 (68)	23 (27)	
BMI	26.5	27.9 ± 7.9	25.7 ± 4.3	
Diabetes mellitus	8	0	8 (10)	
Preoperative MMSE score	28.3	28.9 ± 0.9	28.1 ± 1.5	
Education (y)	12.9	13.7 ± 3.9	12.6 ± 2.9	
Intraoperative data				
Anesthesia duration (min)	232	200 (90)	261 (163)	0.008
FIO_2	0.56	0.55 ± 0.07	0.56 ± 0.05	0.34
SPO_2 (%)	98	98 ± 1	98 ± 1	0.27
$ETCO_2$ (kPa)	4.6	4.7 ± 0.4	4.6 ± 0.3	0.009
Body temperature (°C)	35.9	36.1 ± 0.4	35.8 ± 0.4	<0.001
Systemic hemodynamics				
Heart rate (beats/min)	69	73 ± 15	66 ± 12	0.010
MAP (mm Hg)	75	78 ± 13	73 ± 9	0.014
Sevoflurane concentrations				
$ET_{sevoflurane}$ (%)	1.78	1.98 (0.26)	1.68 (0.37)	<0.001
MAC	0.85	0.94 ± 0.09	0.81 ± 0.12	<0.001
MAC_{age}	0.95	0.89 ± 0.07	0.99 ± 0.14	<0.001
Cerebral hemodynamics				
FVm (cm/s)	44	47 ± 14	42 ± 17	0.062
Mx	0.47	0.41 ± 0.16	0.50 ± 0.18	0.011

Data are presented as n (% within group), or mean ± SD. Duration of anesthesia and ETsevoflurane are presented as median (IQR). BMI indicates body mass index; MMSE, mini-mental state examination; FIO2, inspired oxygen fraction; SPO2, peripheral oxygen saturation; ETCO2, end-tidal carbon dioxide; MAP, mean arterial blood pressure; ETSevoflurane, end-tidal sevoflurane; MAC, minimum alveolar concentration at 1 atmosphere; MACage, age-adjusted minimum alveolar concentration; FVm, mean flow velocity; Mx, index of cerebral blood flow autoregulation. MAP was calculated using a correction factor. MACage was calculated according to MACage = MAC40 x 10−0.00269(age−40).
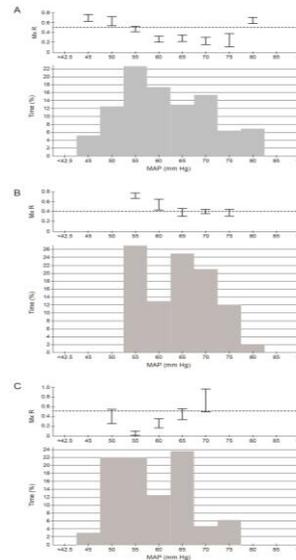

Figure 1. Examples of CBF autoregulation curves (Mx/MAP plots)
A) Patient displaying a "two thresholds" type (Mx limit = 0.5, dotted line).
B) Patient displaying a "lower threshold" type (Mx limit = 0.4, dotted line).
C) Patient displaying an "upper threshold" type (Mx limit = 0.4, dotted line).
CBF indicates cerebral blood flow; Mx, index of cerebral blood flow autoregulation; MAP, mean arterial pressure.
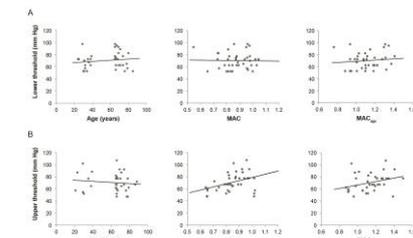

Figure 2. Linear regression plots
A) Lower threshold of CBF autoregulation vs age ($R^2 = 0.0224$, $P = 0.38$), MAC ($R^2 = 0.0009$, $P = 0.86$), and MAC_{age} ($R^2 = 0.0122$, $P = 0.52$).
B) Upper threshold of CBF autoregulation vs age ($R^2 = 0.0094$, $P = 0.57$), MAC ($R^2 = 0.1489$, $P = 0.018$), and MAC_{age} ($R^2 = 0.1049$, $P = 0.050$).
CBF indicates cerebral blood flow; MAC, minimum alveolar concentration at 1 atmosphere; MACage, age-adjusted minimum alveolar concentration.

Table 5. Linear Regression Models of CBF Autoregulatory Thresholds and Mx vs Age, MAC, and MACage

	Lower threshold (n = 38)		Upper threshold (n = 38)		Mx (n = 98)	
	R^2	P	R^2	P	R^2	P
Age	0.0224	0.38	0.0094	0.57	0.0517	0.025
MAC	0.0009	0.86	0.1489	0.018	0.0266	0.12
MAC_{age}	0.0122	0.52	0.1049	0.050	0.0017	0.69

CBF indicates cerebral blood flow; Mx, index of cerebral blood flow autoregulation; MAC, minimum alveolar concentration at 1 atmosphere; MACage, age-adjusted minimum alveolar concentration.

Table 4. Lower and Upper Thresholds of CBF Autoregulation and Autoregulatory Ranges

	Group 1 (≤40 years)	Group 2 (≥65 years)	P
Lower threshold (mm Hg), n = 38	66 ± 12	73 ± 14	0.075
Upper threshold (mm Hg), n = 38	73 ± 19	70 ± 14	0.30
Autoregulatory range (mm Hg), n = 59	13.8 ± 9.8	10.2 ± 8.6	0.079

CBF indicates cerebral blood flow.

Conclusion

Our data shows that the autoregulatory plateau is significantly shortened in both younger and older patients under sevoflurane anesthesia with approximately one MAC. It remains unclear whether this reduction of the human brain's capacity to autoregulate CBF has an impact on the vulnerability for intraoperative cerebral ischemic events.

References

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