Reperfussion Effects After Cerebral Injury

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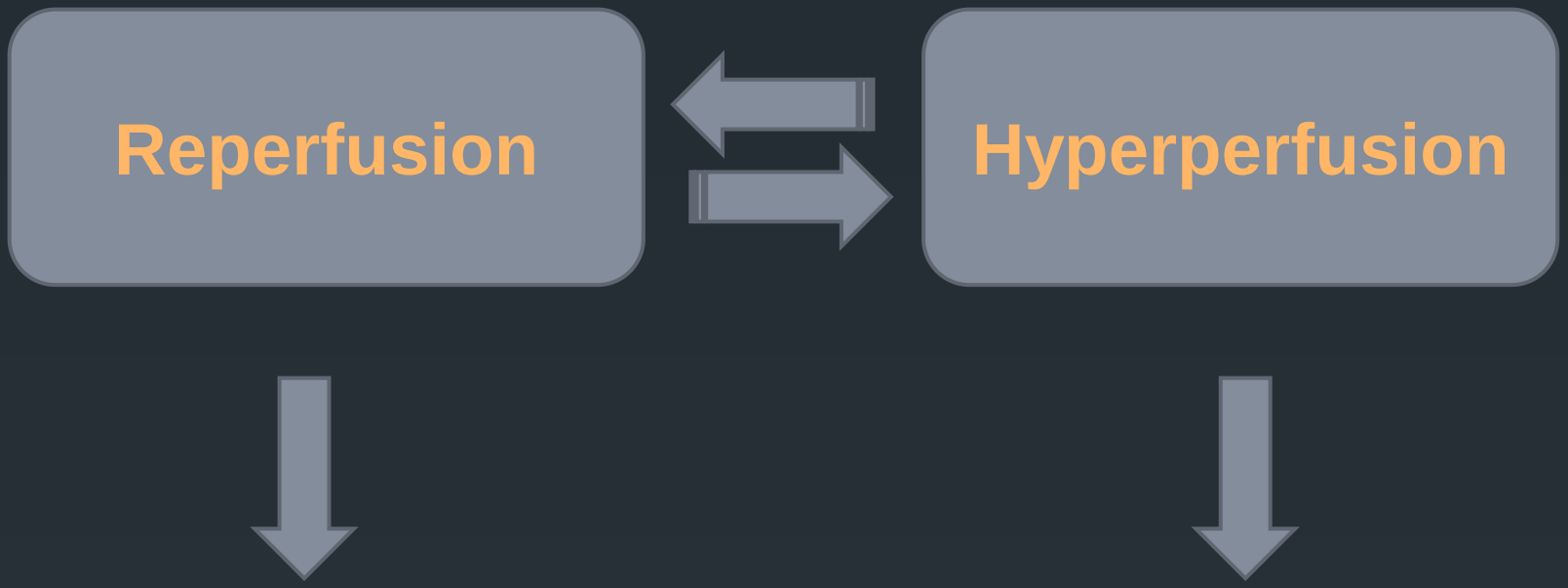

Normalization of the Flow

Excessive Flow

Postcarotid Endarterectomy Hyperperfusion or Reperfusion Syndrome

Theodoros Karapanayiotides, MD; Reto Meuli, PhD; Gerald Devuyst, MD; Bartlomiej Piechowski-Jozwiak, MD; Annelise Dewarrat, MD; Patrick Ruchat, MD; Ludwig Von Segesser, MD; Julien Bogousslavsky, MD

Background and Purpose—Hyperperfusion syndrome (HS) after carotid endarterectomy (CEA) has been related to impaired cerebrovascular autoregulation in a chronically hypoperfused hemisphere. Our aim was to provide new insight into the pathophysiology of the HS using magnetic resonance imaging (MRI) studies with diffusion-weighted imaging (DWI) and perfusion-weighted imaging (PWI).

Methods—Five out of 388 consecutive patients presented 2 to 7 days after CEA, partial seizures (n=5), focal deficits (n=5), and intracerebral hemorrhage (n=3). In 4 patients, using sequential examinations, we identified vasogenic or cytotoxic edema by DWI; we assessed relative interhemispheric difference (RID) of cerebral blood flow (CBF) by PWI; and we measured middle cerebral artery mean flow velocities (MCA Vm) by transcranial Doppler (TCD).

Results—None of the patients presented pathological DWI hyperintensities, consistent with the absence of acute ischemia or cytotoxic edema. In 2 patients, we found an MRI pattern of reversible vasogenic edema similar to that observed in the posterior leukoencephalopathy syndrome. Middle cerebral artery (MCA) mean flow velocities (Vm) were not abnormally increased at any time. PWI documented a 20% to 44% RID of CBF in favor of the ipsilateral to CEA hemisphere.

Conclusions—HS can occur in the presence of moderate relative hyperperfusion of the ipsilateral hemisphere. MCA Vm values may not accurately reflect RID of CBF over the cortical convexity. We suggest that the hemodynamic pathogenetic mechanisms of the HS are more complicated than hitherto believed and that they may be more accurately described by the term "reperfusion syndrome." (***Stroke*****. 2005;36:21-26.)**

Key Words: carotid endarterectomy ■ reperfusion ■ ultrasonography, Doppler, transcranial

Overview

- Early recognition
- Prevention of precipitating factors
  - Hypertension is the most important
- Prognosis following hemorrhagic transformation is poor.
- It is directly related to stroke damage and inflammatory response.
- Damage to the blood brain barier (BBB)

Symptoms

- Cerebral reperfusion syndrome presents as a triad:
  - Ipsilateral headache
  - Contrlateral neurological deficits
  - Seizure
- Symptoms may arise up to one month.

Headache following carotid endarterectomy: a prospective study.

Cephalalgia. 1992; 12(6):380-2 (ISSN: 0333-1024)

Tehindrazanarivelo AD; Lutz G; PetitJean C; Bousser MG
Service de Neurologie, Hôpital Saint-Antoine, Paris, France.

The occurrence of headache in the 28 days following surgery was studied in 50 consecutive patients (14F and 36M, mean aged 70 years) who underwent carotid endarterectomy for atheromatous carotid stenosis. Thirty-one patients (62%) reported headache. Headache occurred in the first five days after surgery in 87% of cases. Its characteristics and temporal profile were highly variable but it was mostly bilateral (74%), mild or moderate (78%), requiring no treatment (77%). No correlation was found between the occurrence of headache and degree of stenosis, intraoperative characteristics and past history of headache. In none of our patients was severe ipsilateral headache, cerebral hyperperfusion syndrome, or cluster-like hemicrania encountered and only five patients met the IHS criteria for post-endarterectomy headache. Post-endarterectomy headache is frequent when specifically looked for and is therefore not a single entity. The present IHS criteria are unsatisfactory and should be modified accordingly.

Seizures After Carotid Endarterectomy: Hyperperfusion, Dysautoregulation or Hypertensive Encephalopathy?

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Objectives: *presentation, management and outcome following seizure after carotid endarterectomy (CEA).*
Materials and Design: *prospective audit.*
Results: *Eight patients (0.8%) suffered a seizure (three bilateral) <30 days following 949 CEAs. Seizure was not associated with age, gender or presentation. Seven were treated hypertensives but four had labile BP pre-operatively. Five had severe bilateral carotid disease and four had vertebral/subclavian stenoses. Six had a >50% drop in middle cerebral artery blood flow velocity (MCAV) with clamping. Only three had >100% increase in MCAV with flow restoration. Five required treatment for post-operative hypertension. Two suffered seizures <36 hrs of CEA, the remainder were at 3–8 days. All eight had significantly elevated blood pressure at onset of seizures. Four underwent immediate MCAV monitoring and each was elevated. Emergency CT scanning/autopsy showed normal scans (n = 3), white matter oedema (n = 3), oedema and diffuse haemorrhage (n = 1), intracranial haemorrhage (n = 1). Seven developed a post-ictal neurological deficit (stroke = 5, TIA = 2). Overall, two patients either died or suffered a disabling stroke.*
Conclusions: *post-CEA seizure was associated with adverse outcome. Most were labile hypertensives with severe bilateral carotid/vertebral disease. MCAV changes suggested poor collateral recruitment, but no consistent pattern of early hyperperfusion emerged. It remains uncertain whether high MCAVs and severe hypertension after seizure onset are cause or effect. Clinicians treating these patients in acute medical units were generally unaware of the "post-CEA hyperperfusion syndrome" and tended to treat the hypertension less aggressively.*

Eur J Vasc Endovasc Surg. 2003 Jul;26(1):39-44

Table 3. Clinical parameters and outcome after onset of seizures.

	Seizure	Neuro deficit	BPOA mmHg	MCAVOA peak/ mean cm/s	Admitted to	CT scan	Outcome
1	4 days *	Hemiparesis	220/170	140/116	Other med	Normal	Hemiparesis recovered <72 h. OHS = 0 at 30 days
2	5 days *	None	206/97	170/93	Vasc unit	Normal	No recurrent seizures, no neurological deficit
3	7 days	None	170/90	n/a	Med unit	Not done	Discharged next day, fatal ICH 26 h later
4	5 days	Hemiparesis	180/80	n/a	On ward	PCO + APH	Hemiparesis recovered <24 h
5	8 days *	Hemiparesis	210/110	n/a	Vasc unit	Normal	Hemiparesis recovered <12 h
6	3 days	Hemiparesis	209/90	n/a	On ward	PCO	Hemiparesis recovered <48 h. OHS = 0 at 30 days
7	32 h	Hemiparesis	220/112	240/174	On ward	ACO + ICH	No significant improvement, OHS 5 at day 30
8	(i) 17 h	Dysphasia	200/150	194/94	On ward	ACO	Dysphasia resolved <24 h. Discharged home on day 7.
	(ii) 8 days	Hemiplegia	142/75	134/74	Other med	ACO	OHS 2 at 30 days

* indicates patients with bilateral seizures, BPOA indicates first BP reading after onset of symptoms, MCAVOA = first MCAV reading after onset of symptoms which may not be the same time as reading BPO. CT reports: PCO = posterior circulation white matter oedema, APH = anterior circulation petechial haemorrhage, ACO = anterior circulation white matter oedema, ICH = intracranial haemorrhage, OHS = Oxfordshire handicap Scale (REF). OHS 0–2 = non-disabling stroke, 3–5 = disabling stroke.

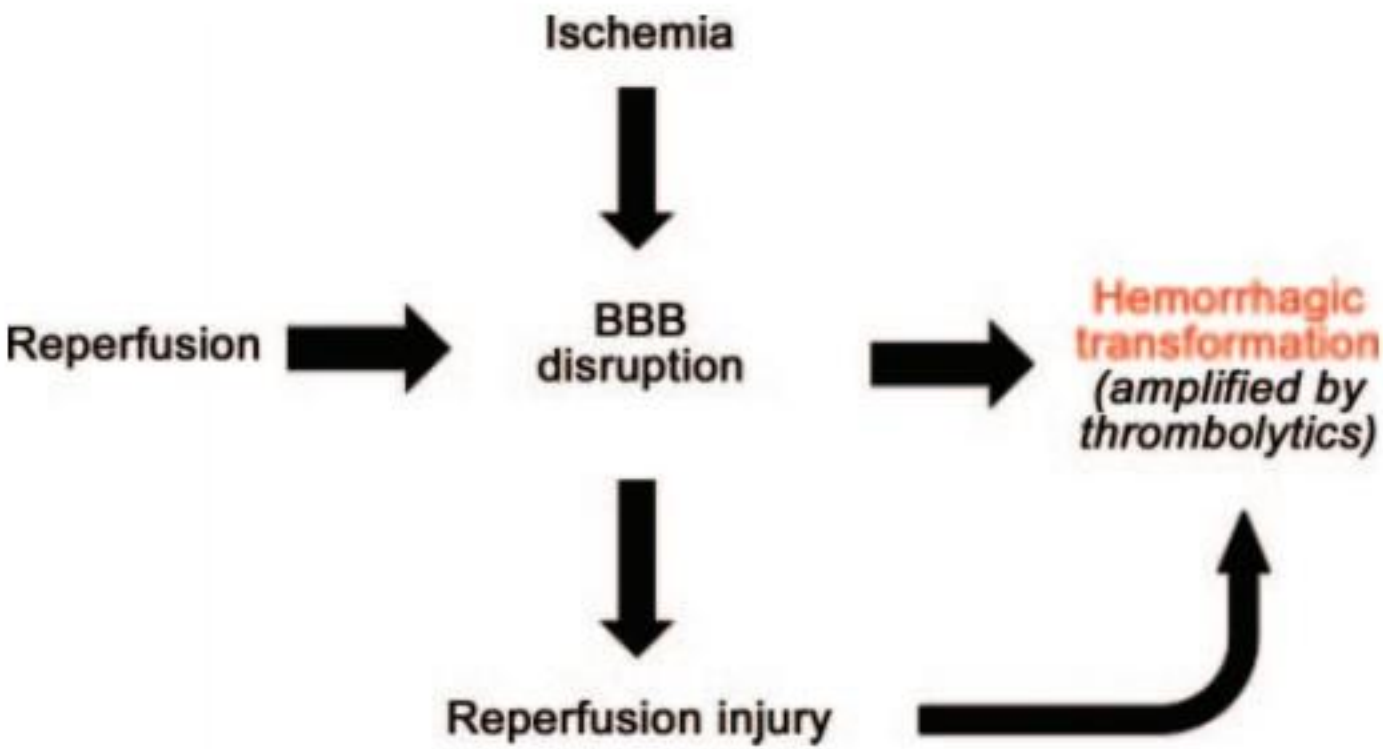
Risk Factors

- Post-operative hypertension
- High-grade stenosis with poor colleteral flow
- Decreased cerebral vasoreactivity
- Increased peak pressure, such as in contralateral carotid occlusion
- Recent contralateral CEA (<3 mo)

Hypertension

- The most common factor
- A physiologic compensation for cerebral ischemia
- The key to reperfusion injury is ischemic disruption of BBB.
- The injured endothelium is unable to maintain its structural integrity against systemic vascular resistance.
  - Reperfusion injury
  - Hemorrhagic transformantion.

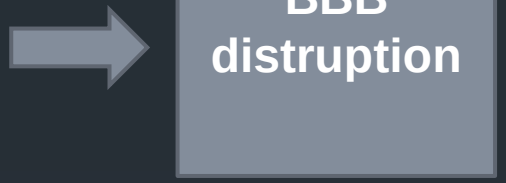
Figure 1 Schematic representation of blood–brain barrier (BBB) changes in acute ischemic stroke



Thrombolytics (IV as well as intra-arterial) can amplify the risk of hemorrhagic transformation secondary to reperfusion injury.

Ischemia

- Lack of glucose and oxygene
- Depletion of ATP
- Decrease in Na-K-ATPase
- Lactic acidosis
- Release of extracellular glutamate



Ischemia

- Endothelial swelling
- Release of proteolytic enzymes leading permeability
- Nitric oxide
- Microvascular leukocyte accumulation
- Proinflammatory cytokines such as interleukin-1 and tissue necrosis factor-α
- Toxic free radicals

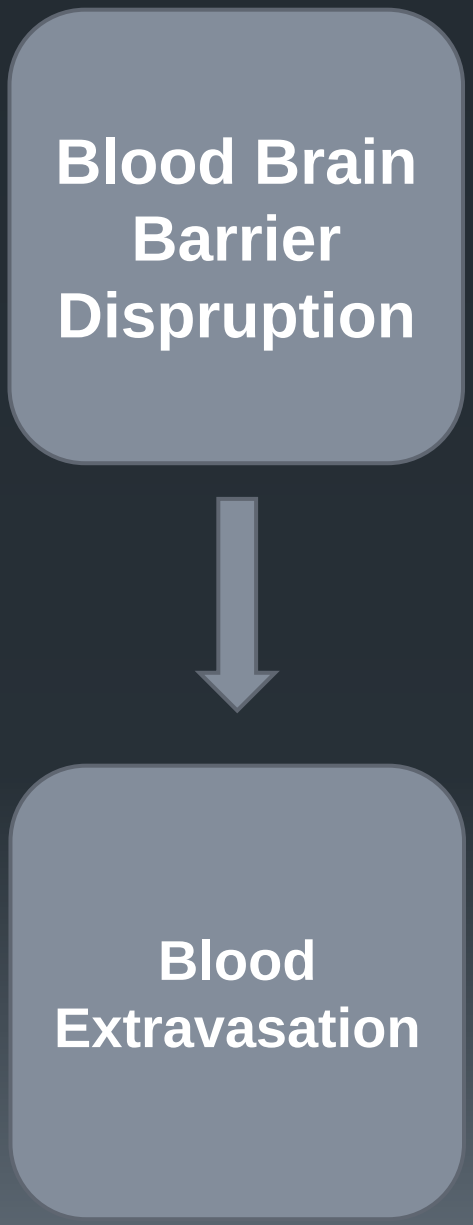
Reperfusion Effects on Brain

- Stage 1. Reactive hypermia leading loss of cerebral autoregulation, increased BBB permeability and acute elevation in regional cerebral blood flow.
- Stage 2. Hypoperfusion
- Stage 3. Paracellular permeability

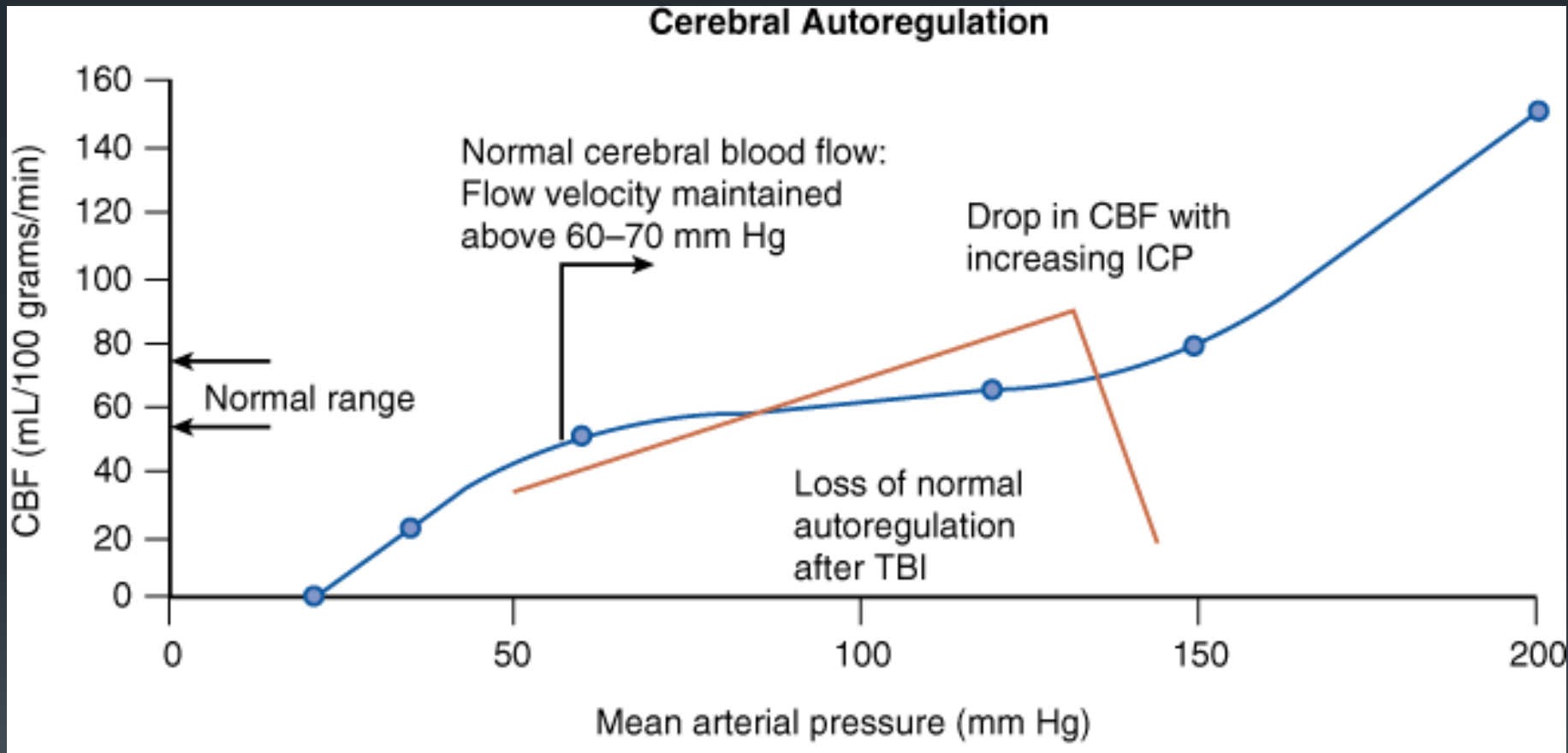
Evidence of Reperfusion Injury, Exacerbated by Thrombolytic Therapy, in Human Focal Brain Ischemia Using a Novel Imaging Marker of Early Blood–Brain Barrier Disruption

Steven Warach, MD, PhD; Lawrence L. Latour, PhD

Abstract—Loss of integrity of the blood–brain barrier (BBB) resulting from ischemia and reperfusion is a hypothesized precursor to hemorrhagic transformation (HT) and worse clinical outcome than would be expected from the beneficial effects of reperfusion. We used a novel magnetic resonance imaging marker to characterize early BBB disruption in acute focal brain ischemia and tested associations with reperfusion, HT, and poor outcome (modified Rankin score >2). The BBB disruption was evident as delayed gadolinium enhancement of cerebrospinal fluid space on fluid-attenuated inversion recovery (FLAIR) images and, for convenience, has been termed hyperintense acute reperfusion marker (HARM). HARM was found in 47 of 144 (33%) ischemic stroke patients. Reperfusion was found to be the strongest independent predictor of early BBB disruption (P=0.018) in multivariate analysis. HARM was associated with HT and worse clinical outcome (after adjustment for initial severity). It was also associated with more severe strokes at onset and greater age. Because the timing of the disruption was early enough (median estimate 3.8 hours from onset) to make it relevant to acute thrombolytic therapy, early BBB disruption as defined by HARM may be a promising target for adjunctive therapy to reduce the complications associated with thrombolytic therapy, broaden the therapeutic window, and improve clinical outcome. (***Stroke***. **2004;35[suppl I]:2659-2661.**)


Blood Brain Barrier Dispruption
Blood Extravasation

Dysautoregulation



Reperfusion Injury After Thrombolytic Therapy

- Within 24-36 hours of stroke after revascularization (lytics, antitrombotics or mechanical devices)
- The question is whether the increased rates of hemorrhagic transformation is related to reperfusion and biochemical pathways or lytic itself?
- Incidence is higher with intra-arterial lytics (10%) than intravenous (6.4%)

Effect of r-tPA

- The hemorrhage may be related to directly thrombotytic
- Thrombolytic may exacerbate BBB distruption
  - Promote the inflamation by NMDA –type glutamate receptors
  - Amplify excitotoxic calcium currents

Risk Factors for Hemorrhagic Transformation

- Stroke severity
- Age (to be older)
- Higher lytic doses
- Delayed revascularization
  - The median time estimate of BBB distruption from onset of ischemia is proposed to be 3.8 hours.

Prevention of Reperfusion Injury

- Blood pressure control
  - What is the optimal blood pressure?

J Neurosurg 68:532–536, 1988

Intracerebral hemorrhage after carotid endarterectomy

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✓ A series of 14 patients with intracerebral hemorrhage after carotid endarterectomy is reviewed. This complication occurred in 0.6% of 2362 consecutive carotid endarterectomies performed at the Mayo Clinic from 1972 through 1986. All hemorrhages occurred within the first 2 weeks after operation and were ipsilateral to the side of the operation. Eight patients died, and only two made a good recovery. Significant risk factors are hypertension and chronic hemispheric hypoperfusion with impaired autoregulation. The "normal pressure-hyperperfusion breakthrough" syndrome was considered to be operative in 12 of the 14 patients. Nine patients had documented hyperperfusion (at least 100% increase of baseline cerebral blood flow) at the time of surgery. In an additional three patients, normal perfusion-pressure breakthrough was inferred by the clinical course and radiological findings, as well as by the absence of alternative explanations. Patients at risk for postendarterectomy intracerebral hemorrhage include those who have a clinical history suggestive of hemodynamic cerebral ischemia, severe carotid stenosis with limited hemispheric collateral flow, and postendarterectomy hyperperfusion, as measured by intraoperative cerebral blood flow. To minimize the risk of hemorrhage in these patients, strict maintenance of blood pressure at normotensive or even relatively hypotensive levels during the intraoperative and early postoperative periods is advised.

KEY WORDS • **intracerebral hemorrhage** • **carotid endarterectomy**

TABLE 1

Clinical summary of patients with postoperative intracerebral hemorrhage

Case No.	Sex & Age (yrs)	Cerebral Ischemia*	Preop < Postop BP†	Preop Angiographic Findings‡	Cerebral Blood Flow		Time: Op to Hemorrhage (days)	Outcome
					Postop Increase (%)	Anesthetic Agent		
1	F, 73	hemodynamic	no	lt ICA stenosis (99%); slow flow; poor collaterals	166	isoflurane	0	poor
2	F, 68	hemodynamic	no	lt ICA stenosis (99%) & rt ICA occlusion; slow flow; poor collaterals	240	isoflurane	2	poor
3	M, 55	contralateral	no	lt ICA stenosis (95%); slow flow; poor collaterals	no change	isoflurane	9	poor
4	F, 74	TIA, (?) embolic	no	rt ICA stenosis (99%); slow flow; moderate collaterals	123	Ethrane	0	poor
5	F, 62	hemodynamic	no	rt CCA occlusion; slow flow; poor collaterals	> 300	Ethrane	9	dead
6	F, 69	hemodynamic	no	rt ICA stenosis (95%); slow flow; poor collaterals	no change	isoflurane	2	dead
7	M, 67	hemodynamic	no	lt ICA stenosis (99%); slow flow; poor collaterals	55	isoflurane	5	dead
8	F, 70	uncertain etiology	no	rt ICA stenosis (75%)	no change	Ethrane	0	dead
9	M, 74	hemodynamic	yes	rt & lt ICA stenosis (99%); slow flow; poor collaterals	184	Ethrane	9	dead
10	M, 72	TIA, (?) embolic	yes	lt ICA stenosis (99%); slow flow; poor collaterals	500	Ethrane	6	dead
11	F, 67	amaurosis fugax, (?) embolic	yes	lt ICA stenosis (99%); slow flow; good collaterals	18	halothane	7	dead
12	M, 77	hemodynamic	yes	rt ICA stenosis (99%); slow flow; good collaterals	579	Ethrane	2	dead
13	M, 77	asymptomatic	not known	lt ICA stenosis (99%); slow flow; poor collaterals	111	halothane	13	good
14	M, 66	hemodynamic	no	lt ICA stenosis (99%); slow flow; poor collaterals	104	isoflurane	0	good

* Hemodynamic means orthostatic cerebral ischemia or orthostatic repetitive involuntary movements. TIA = transient ischemic attack.

† Indicates whether postoperative systolic blood pressure (BP) was greater than maximum preoperative BP and greater than 180 mm Hg systolic.

‡ Percent reduction in internal carotid artery (ICA) caliber.

Intracranial hemorrhage after carotid endarterectomy and carotid stenting in the United States in 2005

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Background: Intracranial hemorrhage (ICH) following carotid endarterectomy (CEA) or carotid artery stenting (CAS) is a rare but potentially devastating complication. The effect of more intense dual antiplatelet therapy required for CAS on the frequency of ICH has not been established. This study was undertaken to evaluate the nationwide occurrence of ICH associated with CAS vs CEA.

Methods: The Nationwide Inpatient Sample was used to identify patients discharged after CAS and CEA during 2005. The type of revascularization and major adverse events, ie, in-hospital ICH, postprocedural stroke, and death rates, were determined by cross-tabulating specific procedural codes for CAS and CEA and diagnostic codes for carotid stenosis. Risk stratification was performed using the Charlson Comorbidity Index. Univariate and multivariate logistic regression analyses were used to assess the association between type of revascularization, comorbidities, ICH, and risk-adjusted mortality.

Results: In 2005, the estimated number of carotid revascularizations was 135,903. The vast majority of patients underwent CEA (90.4%), whereas CAS was performed in 13,093 (9.6%) patients. Most patients (92.2%) underwent treatment for asymptomatic carotid stenosis. CAS patients had higher postoperative stroke rates (2.1% vs 1.1%; $P < .001$) and in-hospital mortality (1.1% vs 0.6%; $P < .001$) than CEA patients. ICH occurred in 19 patients (0.15%) after CAS and in 20 patients (0.016%) after CEA ($P < .001$). CAS was identified as an independent predictor for postoperative stroke (odds ratio [OR], 1.77; 95% confidence interval [CI], 1.5-2.0; $P < .001$), in-hospital mortality (OR, 1.49; 95% CI, 1.2-1.8; $P < .001$) and ICH (OR, 5.9; 95% CI, 3.1-11.1; $P < .001$) after adjusting for age, gender, symptomatic status, comorbidities, admission, and hospital type using logistic regression. In-hospital mortality was 12.5% among patients developing ICH (OR, 23.2; 95% CI, 9.1-54.4; $P < .001$).

Conclusion: In the United States, patients undergoing CAS have not only significantly increased postoperative stroke and death rates compared with those undergoing CEA, but also a sixfold increased risk of ICH. Although ICH after CAS is extremely rare, its devastating nature and high mortality warrant further investigation to define specific risk factors, prevention, and treatment strategies. (J Vasc Surg 2009;49:623-9.)

Table II. Independent predictors of intracranial hemorrhage and death after carotid interventions*

	Coefficient	*Odds Ratio†*	*95% Confidence Interval*	P *value*
Intracranial hemorrhage				
CAS (vs CEA)	1.754	5.90	3.1-11.1	< .001
Age	0.055	1.02	1.01-1.02	.003
Charlson comorbidity index	0.298	1.35	1.1-1.7	.005
Nonelective admission	2.685	14.70	5.8-37.2	< .001
Female gender	1.501	4.49	1.8-11.4	.002
Hypertension	0.688	1.99	1.1-3.9	.044
Renal failure	1.742	5.71	2.4-13.5	< .001
In-hospital mortality				
CAS (vs CEA)	0.398	1.49	1.2-18	< .001
Age	0.013	1.01	1.01-1.02	.001
Charlson comorbidity index	0.312	1.37	1.3-1.4	< .001
Nonelective admission	1.405	4.07	3.5-4.7	< .001
Female gender	0.248	1.28	1.1-1.5	.001
Renal failure	0.651	1.92	1.5-2.4	< .001
Symptomatic carotid stenosis	0.629	1.88	1.6-2.2	< .001
Intracranial hemorrhage	1.388	4.01	1.5-10.9	.007

CEA, carotid endarterectomy; *CAS*, carotid artery stenting.

*Variables with a *P* value < .25 in the univariate analysis and those known to be important and possible confounding factors were entered into the multivariate logistic regression models and selected by forward stepwise selection if *P* value < .05 (*P* < .001 for models).

Risk Factors for Severe Hemorrhagic Transformation in Ischemic Stroke Patients Treated With Recombinant Tissue Plasminogen Activator

A Secondary Analysis of the European-Australasian Acute Stroke Study (ECASS II)

Vincent Larrue, MD; Rüdiger von Kummer, MD; Achim Müller, MSc; Erich Bluhmki, PhD

Background and Purpose—Intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA) improves the outcome for ischemic stroke patients who can be treated within 3 hours of symptom onset. The efficacy of thrombolysis has been demonstrated despite an increased risk of severe hemorrhagic transformation (HT) in patients treated with rtPA. We performed an analysis of risk factors for severe HT in the second European-Australasian Acute Stroke Study (ECASS II).

Methods—HTs were classified by using clinical and radiological criteria as follows: hemorrhagic infarction (HI), parenchymal hemorrhage (PH), and symptomatic intracranial hemorrhage (SICH). Potential risk factors for HT were tested by stepwise logistic regression analysis, including rtPA-by-variable interactions. In addition, the distribution of bad outcome (modified Rankin score 5 to 6) at day 90 was stratified according to each category of HT.

Results—PH and SICH but not HI were associated with rtPA. Also, PH and SICH but not HI were more severe in rtPA-treated patients than in those receiving placebo. Risk factors for PH were rtPA, extent of parenchymal hypoattenuation on baseline CT, congestive heart failure, increasing age, and baseline systolic blood pressure. The risk of PH on rtPA was increased in older patients and in those who were treated with aspirin before thrombolysis. Risk factors for SICH were rtPA, congestive heart failure, extent of parenchymal hypoattenuation, and increasing age. The risk of SICH on rtPA was increased in patients who were treated with aspirin before thrombolysis.

Conclusions—This secondary analysis of ECASS II has confirmed the importance of the extent of hypoattenuation as a risk factor for severe HT. The findings also suggest that older patients and those who have used aspirin before stroke are at higher risk of a severe HT on rtPA. (*Stroke*. **2001;32:438-441.**)

Key Words: intracerebral hemorrhage ■ risk factors ■ stroke, acute ■ thrombolytic therapy

TABLE 1. Distribution of HT Between Treatment Groups

Category of HT	Placebo Group (N=386)	rtPA Group (N=407)
No HT, n (%)	233 (60.4)	217 (53.3)
HI, n (%)	141 (36.5)	142 (34.9)
PH, n (%)	12 (3.1)	48 (11.8)
SICH, n (%)	13 (3.4)	36 (8.9)

TABLE 3. Final Logistic Model Regarding the Association of Baseline Variables with PH

Variable	Odds Ratio	95% CI	*P*
rtPA	3.61	1.78–7.31	<0.0001
Attenuation of density on baseline CT	2.64	1.59–4.39	<0.001
Prior congestive heart failure	2.57	1.16–5.71	0.02
Baseline systolic blood pressure	1.02	1.00–1.03	0.02
Age	1.04	1.00–1.08	0.04
Aspirin	1.26	0.55–2.92	0.06
Age+rtPA	1.07	0.99–1.15	0.05
Aspirin rtPA	4.99	0.91–27.4	0.06

P≤0.06 for enter and stay criteria.

Free-radical Scavengers and Antiadhesion Therapy

- Agents that block leukocyte endothelial adhesion
  - Monoclonal antibodies that block adhesion receptors either on leukocytes (CD-18) or the endothelial cell (ICAM-1)
- Experimental studies have shown beneficial effects

Free-radical Scavengers and Anti-adhesion Therapy

- Anti-adhesion therapies is beneficial when reperfusion is likely and not beneficial when the ischemia is permenant.
- Clinical studies using anti-bodies against ICAM-1 have failed to show clinical benefit.

Pretreatment with the Free Radical Scavenger Edaravone Prevents Cerebral Hyperperfusion after Carotid Endarterectomy

OBJECTIVE: Cerebral hyperperfusion syndrome after carotid endarterectomy (CEA) is a rare but potentially devastating complication. The purpose of the present study, which was not a randomized controlled trial but a case cohort study with historical control, was to determine whether pretreatment with a novel free radical scavenger, edaravone, could prevent occurrence of cerebral hyperperfusion after CEA.

METHODS: Fifty patients with ipsilateral internal carotid artery stenosis (≥70%) underwent CEA with administration of edaravone before internal carotid artery clamping. Preoperative cerebral blood flow and cerebrovascular reactivity (CVR) to acetazolamide were assessed with single-photon emission computed tomography (SPECT). Cerebral blood flow also was measured immediately after CEA and on the 3rd postoperative day.

RESULTS: Cerebral hyperperfusion (cerebral blood flow increase ≥100% compared with preoperative values) was revealed by SPECT performed immediately after CEA in only one patient (2%), who also exhibited reduced preoperative CVR. The incidence of post-CEA hyperperfusion as revealed by SPECT in the control group (51 CEA patients without administration of edaravone) was significantly higher (16%) ($P = 0.0310$, control versus treatment group). In addition, in a subgroup of patients with reduced preoperative CVR, the incidence of post-CEA hyperperfusion as revealed by SPECT in the edaravone group (7%) was significantly lower than that in the control group (67%) ($P = 0.0029$). Logistic regression analysis demonstrated that reduced preoperative CVR and absence of pretreatment with edaravone were significant independent predictors of post-CEA hyperperfusion as revealed by SPECT.

CONCLUSION: Pretreatment with edaravone can prevent occurrence of cerebral hyperperfusion after CEA.

KEY WORDS: Carotid endarterectomy, Cerebral hyperperfusion, Free radical scavenger

Neurosurgery 55:1060-1067, 2004 DOI: 10.1227/01.NEU.0000140838.27450.63 www.neurosurgery-online.com

TABLE 1. Patient characteristics of the control and edaravone groups[a]

Patient characteristics	Edaravone (n = 50)	Controls[b] (n = 51)	*P* value
Age (yr) (mean ± SD)	69.2 ± 4.9	68.2 ± 5.9	NS
Male sex	42	44	NS
Hypertension	44	38	NS
Diabetes mellitus	17	15	NS
Symptomatic lesion	36	27	NS
Infarction on MRI scan	27	26	NS
Bilateral lesions	16	16	NS
Degree of ICA stenosis (%) (mean ± SD)	83.9 ± 7.4	84.1 ± 7.7	NS
Poor collateral circulation	16	19	NS
Duration of ICA clamping (min) (mean ± SD)	33.0 ± 4.0	32.3 ± 6.8	NS
Reduced CVR	14	12	NS

[a] SD, standard deviation; MRI, magnetic resonance imaging; ICA, internal carotid artery; CVR, cerebrovascular reactivity to acetazolamide; NS, not significant.
[b] Controls were reported previously (19).

TABLE 2. Incidence of hyperperfusion after carotid endarterectomy as revealed by single-photon emission computed tomography in the control and edaravone-treated groups[a]

Denominator	Edaravone	Controls	*P* value
All patients	1/50 (2%)	8/51 (16%)	0.0310
Patients with reduced CVR	1/14 (7%)	8/12 (67%)	0.0029

[a] CVR, cerebrovascular reactivity to acetazolamide.

TABLE 3. Risk factors for hyperperfusion as revealed by single-photon emission computed tomography immediately after carotid endarterectomy[a]

Variables	Hyperperfusion		*P* value
	Yes (n = 9)	No (n = 92)	
Age (yr) (mean ± SD)	68.7 ± 6.9	68.7 ± 5.3	NS
Male sex	8	78	NS
Hypertension	6	76	NS
Diabetes mellitus	2	30	NS
Symptomatic lesion	6	57	NS
Infarction on MRI scan	6	47	NS
Bilateral lesions	5	27	NS
Degree of ICA stenosis (%) (mean ± SD)	90.9 ± 9.7	83.2 ± 7.7	NS
Poor collateral circulation	7	28	NS
Duration of ICA clamping (min) (mean ± SD)	30.2 ± 7.1	32.9 ± 5.4	NS
Reduced CVR	9	17	<0.0001
Pretreatment with edaravone	1	49	0.0139

Thanks