Hyperperfusion Syndrome: Toward a Stricter Definition

OBJECTIVE: Hyperperfusion syndrome is a rare and potentially devastating complication of carotid endarterectomy or carotid artery angioplasty and stenting. With the advent of new imaging techniques, we reviewed our experience with this phenomenon.

METHODS: This report is a retrospective review of 129 consecutive cases of carotid endarterectomy performed between June 1, 2000, and May 31, 2002, and 44 consecutive cases of carotid artery angioplasty and stenting performed between January 1, 1997, and May 31, 2002. We specifically searched for examples of patients who developed post-procedural nonthrombotic neurological deficits that typified the hyperperfusion syndrome.

RESULTS: Seven cases of hyperperfusion syndrome occurred, four after endarterectomy (3.1% of carotid endarterectomy cases) and three after stenting (6.8% of stenting cases). The cases of hyperperfusion were classified as presenting with 1) acute focal edema (two cases with stroke-like presentation, attributable to edema immediately after revascularization), 2) acute hemorrhage (two cases of intracerebral hemorrhage immediately after stenting and one case immediately after endarterectomy), or 3) delayed classic presentation (two cases with seizures, focal motor weakness, and/or late intracerebral hemorrhage at least 24 hours after endarterectomy).

CONCLUSION: Hyperperfusion syndrome may be more common and more variable in clinical presentation than previously appreciated.

KEY WORDS: Carotid artery stenting, Carotid endarterectomy, Hyperperfusion syndrome, Magnetic resonance imaging

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yperperfusion syndrome is reported as a rare but potentially devastating postoperative complication of carotid endarterectomy or carotid artery angioplasty and stenting. Hyperperfusion syndrome was initially described by Sundt et al. (25), in 1981, as a clinical syndrome involving atypical migrainous phenomena, transient focal seizure activity, and intracerebral hemorrhage after carotid endarterectomy. Initially described in association with open carotid artery surgery, this condition has more recently been observed after endovascular carotid artery angioplasty and stenting (4, 10, 15–20). These descriptions have been similar to those of the condition after carotid endarterectomy, with resultant intracerebral hemorrhage, headaches, or seizures, but the overall outcomes seem worse. Among the case reports noted, the risk of death seems high, especially in the presence of intracerebral hemorrhage. It has been presumed that these cases of intracerebral

hemorrhage are related to sudden elevations in cerebral blood flow, but experimental evidence is lacking. Hyperperfusion syndrome seems not to be limited to endovascular interventions involving the large proximal vasculature, because it was recently observed after distal intracranial middle cerebral artery angioplasty (14).

In this report, we present data on seven cases of hyperperfusion syndrome or suspected hyperperfusion syndrome observed among a series of 173 consecutive patients who underwent carotid artery revascularization. The report discusses the clinical and radiological manifestations of the condition, with suggestions for enhancing the clinical diagnosis and treatment.

PATIENTS AND METHODS

One hundred twenty-nine consecutive carotid endarterectomy cases performed between June 1, 2000, and May 31, 2002, and 44

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consecutive carotid artery angioplasty and stenting cases performed between January 1, 1997, and May 31, 2002, were retrospectively reviewed. All procedures were performed at a single tertiary care center, which serves a population of 1.4 million. Examples of hyperperfusion syndrome typified by the development of a nonthrombotic hemispheric neurological deficit after revascularization were identified. Patient charts were examined to determine the rates of perioperative and postoperative complications before hospital discharge.

Carotid endarterectomies were performed by four neurosurgeons, using standard techniques. General anesthesia was used for 117 cases and regional anesthesia for 12. All patients received a bolus of 5000 units of heparin before crossclamping. No surgeon used carotid artery patching or shunting. Plaque removal and vessel suturing were performed with magnification. All patients were monitored in a dedicated neurological unit, with a high level of nursing support for treatment of neurological or hemodynamic problems, during the acute postoperative phase.

Carotid artery angioplasty and stenting were performed by four neurointerventionalists. All patients were considered to be at high surgical risk. Double-antiplatelet therapy (aspirin and ticlopidine or aspirin and clopidogrel, if tolerated) was prescribed for all patients before stenting. Preliminary diagnostic cerebral angiograms were obtained for all patients. Procedures were conducted with local anesthesia, with standard monitoring by an anesthetist. Patients underwent standard femoral artery puncture and placement of 6- or 7-French guiding sheaths. Heparin was administered intravenously, with monitoring of activated coagulation times to maintain a value of at least 250 seconds. An exchange-length guidewire (predominant size, 0.018 inch) was used to cross the lesion. Atropine was administered for treatment of symptomatic bradycardia. Predilation of the stenotic plaque was performed with a low-profile, compliant, angioplasty balloon. Selfexpanding stents (Wallstent; Boston Scientific/Medi-tech, Natick, MA) were used in this case series. Postdilation was performed with a noncompliant angioplasty balloon, at the discretion of the interventionalists. Distal protection devices were available on a compassionate basis from November 2000 onward and were used for seven of the latter patients. Standard angiographic projections of the neck and head were obtained immediately after stenting, for assessment of the technical results and detection of local and distal complications. All patients were monitored after stenting, in the same unit as patients who underwent endarterectomy.

Patient data were qualitatively analyzed by a group of neurologists and neurosurgeons. Each hyperperfusion syndrome case was reviewed by a neuroradiologist, who searched for evidence of intracranial collateral vascular supply. Natural groupings of disease presentations were clustered. Hyperperfusion syndrome was defined as a neurological deficit that occurred after cerebral revascularization and was localized ipsilateral to the treated artery, not related to thromboembolism. Intracerebral hemorrhage and cerebral edema were confirmed with computed tomographic (CT) and/or magnetic resonance imaging (MRI) scans. Seizures were characterized clinically and with electroencephalography. In one case, perfusion imaging findings were available to demonstrate hyperemia of the affected hemisphere. Proportions are reported with exact confidence intervals. Comparisons of clamp times were made by using unpaired, two-tailed, Student's t tests.

RESULTS

Four patients (3.1% of carotid endarterectomy cases; 95% confidence interval, 0.85-7.7%) experienced hyperperfusion syndrome after carotid endarterectomy, and another three patients (6.8% of stenting cases; 95% confidence interval, 1.4-18.7%) experienced hyperperfusion syndrome after carotid artery angioplasty and stenting (Table 1). In the carotid artery angioplasty and stenting group, in addition to the patients with hyperperfusion syndrome, two patients experienced minor embolic strokes and one patient experienced stent thrombosis, which resulted in a minor stroke (the patient could not tolerate clopidogrel or ticlopidine). In the carotid endarterectomy group, there was no statistically significant difference in mean clamp times between the patients with hyperperfusion syndrome (31.5 min) and those without hyperperfusion syndrome (32.0 min; P = 0.93). The overall incidence of stroke or death was 6.2% (95% confidence interval, 2.7-11.8%) for our carotid endarterectomy cases; this included four embolic complications (3.1%; 95% confidence interval, 0.85-7.7%) before hospital discharge. Two patients were successfully treated for pulmonary edema without myocardial infarction. We categorized our hyperperfusion syndrome cases into three types, on the basis of clinical presentation, i.e., 1) acute focal edema, 2) acute hemorrhage, or 3) delayed classic presentation. These types are illustrated below.

Illustrative Cases

Patient 1, with Acute Focal Edema after Carotid Endarterectomy

A 73-year-old man underwent left carotid endarterectomy for treatment of symptomatic 90% stenosis of the left internal carotid artery. His symptoms included multiple transient ischemic attacks and a left hemispheric stroke 3 months previously. There was no contralateral stenosis. The procedure proceeded routinely, and the patient awoke with right hemiplegia and global aphasia. Brain CT scans initially demonstrated sulcal effacement over the left hemisphere (Fig. 1), with no evidence of hemorrhage. Formal angiography was performed immediately and demonstrated that the left internal carotid artery and all intracranial vessels were patent, without emboli. Angiography demonstrated an incomplete circle of Willis; the left hemisphere exhibited reduced collateral flow. Transcranial Doppler ultrasonography (TCD) demonstrated normal mean flow velocities and resistance indices in the major intracranial arteries. Three-tesla MRI scans obtained within 3 hours after awakening of the patient from anesthesia yielded normal results, including relative mean transit time and cerebral blood volume assessments and diffusion-weighted imaging findings. The patient underwent intubation and was admitted to the intensive care unit. Despite the use of four antihypertensive agents to keep his blood pressure well controlled, the patient developed refrac-

Patient no.	Subtype	Age (yr)/sex	Affected artery stenosis	Contralateral artery stenosis	Procedure	3-mo outcome (Rankin scale)	Circle of Willis collaterals
1	Acute focal edema	73/M	90% left ICA	No significant stenosis	E	Independent	No AComA, no left PComA
2	Acute focal edema	70/F	90% left ICA	50%	S	Independent	No AComA, left PComA
3	Acute hemorrhage	71/M	99% left ICA	No significant stenosis	S	Death	AComA, no PComA
4	Acute hemorrhage	62/F	95% right ICA	90%	S	Death	Small AComA, smal right PComA
5	Acute hemorrhage	50/F	99% left ICA	30%	E	Independent	Large AComA, small left PComA
6	Delayed classic	82/F	90% left ICA	99%	E	Independent	Unable to determine
7	Delayed classic	60/M	95% right ICA	50%	E	Death	Small AComA, smal right PComA

^a ICA, internal carotid artery; AComA, anterior communicating artery; PComA, posterior communicating artery; E, carotid endarterectomy; S, carotid artery angioplasty and stenting.

tory hypertension, with systolic blood pressure fluctuating near 200 mm Hg. The patient remained densely hemiplegic, and a CT perfusion study of the brain was performed 48 hours after surgery, during the period of refractory hypertension (*Fig. 1*). Quantitative cerebral blood flow maps demonstrated severely increased cerebral blood flow over the affected hemisphere, confirming the diagnosis of hyperperfusion syndrome. There was no evidence of diffusion-weighted changes on repeat 3-T MRI scans, and the patient made a gradual neurological recovery. At 3 months, he demonstrated mild expressive aphasia and mild hemiparesis.

Patient 2, with Acute Focal Edema after Angioplasty

A 70-year-old woman underwent attempted carotid artery angioplasty and stenting for treatment of symptomatic 90% stenosis of the left internal carotid artery. Her presenting symptoms were severe right hand weakness and very mild right hemiparesis attributable to a discrete motor strip infarction. The patient was considered a poor surgical candidate because of multiple comorbid diseases. Stent deployment was not technically possible, because of tortuous arterial anatomic features, and the patient underwent left internal carotid artery angioplasty only. Immediately after angioplasty, the patient exhibited neurological deterioration and developed right hemiparesis and global aphasia, which worsened during a 60-minute period. Angiography demonstrated no evidence of large- or small-vessel occlusion. Brain CT scans demonstrated diffuse hypoattenuation of the left hemisphere in all vascular territories, with swelling interpreted as vasogenic edema. During the procedure, the patient exhibited blood pressure as high as 220/120 mm Hg. TCD demonstrated no elevation of middle cerebral artery mean flow velocities. The patient was admitted to the intensive care unit, her blood pressure was aggressively maintained at 130/90 mm Hg, and she exhibited gradual improvement. Her speech returned to normal and she was left with mild

residual right hemiparesis, consistent with her original stroke. At the 3-month follow-up visit, the patient was asymptomatic.

Patients 3, 4, and 5, with Acute Intracerebral Hemorrhage

A 71-year-old man underwent left carotid artery stenting for treatment of symptomatic 99% stenosis of the left internal carotid artery (Patient 3 is described; see *Table 1* for data on Patients 4 and 5). Two months previously, the patient had presented with left hemispheric transient ischemic attacks followed by a minor stroke, which left him with mild right arm weakness. He was considered a poor surgical candidate because of multiple comorbid illnesses. Stenting was uneventful, with good technical results. The patient's blood pressure was controlled during the procedure, and there was no evidence of poststenting hypertension. Three hours after the procedure, the patient suddenly developed rightside hemiplegia and aphasia. Brain CT scans demonstrated a large deep hematoma in the left hemisphere (*Fig. 2*), as a result of which the patient died. An autopsy confirmed massive left hemispheric hemorrhage, with secondary lateral and central herniation.

Patients 6 and 7, with Delayed Classic Presentation

An 82-year-old woman underwent left carotid endarterectomy for treatment of symptomatic 90% stenosis of the left internal carotid artery (Patient 6 is described; see *Table 1* for data on Patient 7). The patient presented with several transient ischemic attacks and a minor stroke, which left her with some mild expressive aphasia. Carotid endarterectomy proceeded uneventfully, and no intraoperative blood pressure problems were encountered. During the subsequent few days, the patient developed mild hypertension (145/84 to 180/94 mm Hg); she awoke on the sixth postoperative day with right arm weakness and increasing word-finding difficulties. CT scans demonstrated edema and loss of gray matter/white matter differentiation in the left hemisphere (*Fig. 3*). CT angiography of the circle of Willis demonstrated

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that the extracranial internal carotid artery and all major intracranial vessels were patent, with no obvious thrombus. TCD demonstrated normal middle cerebral artery mean flow velocities and resistance indices. MRI scans confirmed the presence of vasogenic edema affecting the left hemisphere (Fig. 3). Despite aggressive blood pressurelowering therapy, 3 days later the patient experienced a tonicoclonic seizure and underwent intubation. The patient remained in the intensive care unit for 2 weeks; with aggressive blood pressure-lowering therapy, she gradually recovered to her baseline condition.

DISCUSSION

Definition

The term hyperperfusion syndrome was initially used to describe the presentation of focal seizures and intracerebral hemorrhage a few days after carotid endarterectomy (25). A broad range of symptoms and clinical findings are associated with hyperperfusion syndrome. Many of our cases involved presentations different from the original description. We propose a redefinition of hyperperfusion syndrome as a hemispheric neurological deficit (or seizure) occurring after cerebral revascularization, localized ipsilateral to the treated artery, not related to thromboembolism, and without evidence of new infarction on diffusionweighted MRI scans. Perfusion MRI or CT scans should demonstrate the existence of hyperperfusion in the ipsilateral hemisphere. Not all of the cases met this stricter definition, because of the evolution of our approach to such cases. Quantification is important for the future evaluation of hyperperfusion syndrome, because it is clear that the presence of a neurological deficit alone cannot



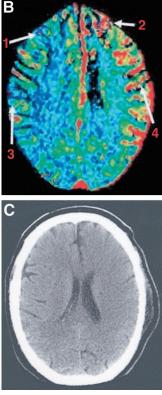


FIGURE 1. Patient 1. A, CT scan obtained immediately postoperatively, showing sulcal effacement over the left hemisphere. B, CT perfusion scan obtained at 4 days, with the cerebral blood flow map. Regions of interest were indicated on the cerebral blood flow map, and exact values for cerebral blood flow were recorded for the regions (Region 1, 25 ml/100 g/min; Region 2, 77 ml/100 g/min; Region 3, 14 ml/100 g/min; Region 4, 63 ml/100 g/min). C, CT scan obtained at 4 days, showing edematous change in the left hemisphere, with loss of the gray matter/white matter border. establish the cause. This was a retrospective case series; as our knowledge of this disease increased, our protocol began to include quantitative assessments of perfusion. We postulate that there are three distinct subtypes of hyperperfusion syndrome, as described in this report, but we advise caution in the generalization of these results to the population as a whole.

One potential weakness of our study is the fact that we did not completely exclude the possibility of thromboembolic infarction with delayed hemorrhage. However, in the two cases that occurred after stenting, the hemorrhage occurred acutely. The vessel was patent at the end of the procedure, and infarction with subsequent hemorrhage within 1 hour seems unlikely.

Pathophysiological Features

The pathophysiological mechanism of cerebral hyperperfusion syndrome remains unclear. Traditional teaching has been that hyperperfusion syndrome is attributable to the failure of normal cerebral autoregulation, secondary to long-standing changes in perfusion pressure. Maximal dilation of cerebral arterioles for long periods of time causes loss of cerebral blood flow autoregulation in areas of chronically underperfused brain tissue and can result in hemorrhage and/or edema. The absence of evidence of infarction on acute diffusionweighted MRI scans and the absence of evidence of arterial occlusion argue against the hypothesis that hyperperfusion syndrome is simply a manifestation of postoperative thromboembolic stroke. Hem-



FIGURE 2. Patient 3. A and B, lateral projections of left common carotid artery injections. A, angiogram, showing severe left internal carotid artery stenosis, with the string sign. B, angiogram, showing the left internal carotid artery after angioplasty and stenting. C, brain CT scan, demonstrating left hemispheric intracerebral hemorrhage, a midline shift, and hydrocephalus.

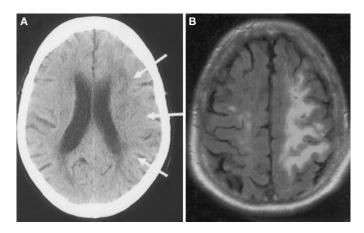


FIGURE 3. Patient 6. A, brain CT scan obtained 6 days after endarterectomy, demonstrating left hemispheric edema (arrows). B, fluid-attenuated inversion recovery MRI scan, confirming the presence of edema in the left hemispheric white matter.

orrhage may be related to a sudden increase in blood flow to the ipsilateral hemisphere and is not necessarily related to a prior or perioperative stroke.

Large series of extracranial carotid artery angioplasty and stenting cases have revealed incidences of stroke and death of 3.6 to 7.9% (6, 27). The 6.8% incidence of hyperperfusion syndrome observed in this study with carotid artery angioplasty and stenting is comparable to the 5% incidence reported by Meyers et al. (16). However, the latter series included a large number of posterior circulation procedures. The true incidence of hyperperfusion syndrome after carotid endarterectomy is unclear, because of the wide variety of symptoms reported, but incidences of up to 9% have been reported, on the basis of perioperative noninvasive TCD results (5, 7).

Risk Factors for Hyperperfusion Syndrome

Risk factors for hyperperfusion syndrome may include severe stenosis or bilateral carotid artery stenosis, previous stroke, periprocedural hypertension, and poor collateral blood supply (2, 9, 15, 21, 23). Two of our patients demonstrated no collateral flow between hemispheres, and many of the others demonstrated limited collateralization via the circle of Willis. There was no relationship between cross-clamp times and hyperperfusion syndrome, but the number of cases was small. Data from the North American Symptomatic Carotid Endarterectomy Trial suggested that the presence of intracranial collateral vascular supply is associated with a lower risk of all types of hemispheric stroke (8). That report hypothesized that a functionally "stressed" cerebral microcirculation might be a marker of risk for hyperperfusion syndrome. The use of anticoagulant agents, preprocedural cerebral infarctions, and preexisting hypertensive microangiopathy might be additional risk factors for intracranial hemorrhage once hyperperfusion syndrome exists (9, 13). Aggressive antiplatelet therapy is often used to prevent stent thrombosis (3, 24), and recent experience with the periprocedural use of glycoprotein IIb/ IIIa inhibitors has been reported (12, 22, 26). As demonstrated in this report, the acute intracerebral hemorrhage variant of hyperperfusion syndrome might be more common with carotid artery angioplasty and stenting, because of the emphasis on antithrombotic regimens with endovascular interventions.

Diagnosis and Treatment

The diagnosis of hyperperfusion syndrome has changed with the advent of new technology. With new imaging procedures, such as perfusion MRI or CT scanning, hyperperfusion syndrome can be rapidly identified. Patients at high risk for hyperperfusion syndrome can be identified by artificially increasing the cerebral blood flow (11) before surgery or intervention. TCD has been advocated by some for the early identification of hyperperfusion syndrome (1, 20), but in our study TCD was unreliable. TCD can be used to identify any early hemodynamic alterations in mean flow velocity (13), but the use of TCD before the procedure is not a sensitive marker for postprocedural hyperperfusion syndrome.

The treatment of hyperperfusion syndrome is currently empirical. Among our patients, aggressive control of blood pressure was associated with clinical and radiological improvement. With a gradual trend toward noninvasive preoperative assessment of carotid artery stenosis, it might be useful to perform formal angiography for patients with critical stenosis or bilateral disease, to search for collateral blood supply. This approach could be formally tested in a clinical trial.

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COMMENTS

Bernstein et al. (1) first introduced the concept of cerebral hyperperfusion after carotid endarterectomy in an exceptional clinicopathological case report that was published in *Neurosurgery* in 1984. They described a normotensive patient who underwent repair of critical, flow-limiting carotid stenosis that was followed by postoperative unilateral head, face, and eye pain; convulsions; and, on the sixth day, fatal intracerebral hemorrhage. Pathological examination of the hemisphere ipsilateral to the endarterectomy revealed changes resembling those seen in malignant hypertension, and the compelling theory proposed was that carotid repair in this patient had resulted in relative hyperperfusion of a vascular bed with impaired autoregulation, causing pain, seizures, and then hemorrhage. Fortunately, intracerebral hemorrhage due to this or any other phenomenon is a rare complication after carotid endarterectomy. In the 1415 surgical patients studied in the North American Symptomatic Carotid Endarterectomy Trial (2), there were only 2 intracerebral hemorrhages. In addition, in a review of 700 consecutive patients, my colleagues and I (3) found only 1 intracerebral hemorrhage, which was delayed and bled into a previously infarcted territory.

The present report by Coutts et al. suggests that on the basis of a somewhat broader definition ("neurological deficit that occurred after cerebral revascularization and was localized ipsilateral to the treated artery"), post-carotid repair cerebral hyperperfusion is relatively common, occurring in 4 (3.1%) of 129 of their endarterectomy cases and 3 (6.8%) of 44 of their angioplasty and stenting cases. Just two of these seven patients had the classic presentation described by Bernstein et al. (1), and only one had hyperemia on the basis of perfusionweighted imaging. It is not entirely clear that cross-clamp ischemia or simple hemorrhagic infarction could not be responsible for some of the other cases, so the authors may have cast their net rather widely. Also not easily explained is the pathophysiology underlying profound neurological deficit and hyperemia (in the absence of hemorrhage). Nevertheless, the authors force readers to think, and they raise the valid point that important information might be obtained from diffusion-weighted magnetic resonance imaging (MRI) and cerebral perfusion pressure studies in patients with apparent stroke after carotid endarterectomy, although the first priority is to rule out more common and sometimes correctable thrombotic or thromboembolic ischemia.

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n this article, the authors examine the conditions in which neurological deficit and hemorrhage occur after carotid reperfusion is administered through endarterectomy or angioplasty. On the basis of their review of 7 cases that occurred after 129 consecutive carotid endarterectomies and 44 consecutive carotid angioplasties, they found 3.1 and 6.8% rates of hyperperfusion syndrome. The difficulty lies in defining hyperperfusion syndrome. The authors define hyperfusion syndrome broadly as a

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neurological deficit occurring after cerebral revascularization localized ipsilaterally to an operative artery and not related to thromboembolic or new MRI-proved infarction. The authors correctly point out that several pathophysiologies of acute neurological demise are probably lumped together under this definition. The classic definition of Sundt et al. (1) described focal seizures and intracranial hemorrhage days postendarterectomy. The present, much broader definition includes various causes, which confuses treatment options. The assumption is that this would show hemispheric increase on perfusion-weighted MRI or computed tomographic scans.

The authors define hyperperfusion syndrome on the basis of the assumption that other causes are excluded. They think that in some cases they have radiographic evidence to exclude some pathophysiologies, such as emboli, and that in other cases the data are suggestive of edema or increased perfusion. However, this evidence is anecdotal. The authors' data would be strengthened greatly by more quantification of perfusion. Furthermore, the authors do not convincingly rule out thromboembolic infarct with delayed hemorrhage, but they do make a good point that MRI perfusion- or diffusion-weighted scans will be the hallmark of this definition in the future. Any further information that the authors could provide on the basis of quantifiable perfusion data would be invaluable in defining this syndrome, because it is clear that the presence of a neurological defect alone cannot determine the outcome of treatment. Such data would move the diagnosis from one of exclusion to one based on clear pathophysiological information.

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The authors report their retrospective experience in treating patients with a rare complication of nonthromboembolic syndrome after carotid revascularization procedures. This phenomenon can occur after both carotid endarterectomy and endovascular stenting. Hyperperfusion syndrome, initially described by Sundt et al. (1), can be more defined precisely with the advent of imaging. All the patients reported to have this complication had minor strokes in their presenting history, suggesting that prior minor stroke may be a risk factor for hyperperfusion syndrome. Without proper statistical analysis, however, it is not possible to confirm such a relationship. In this report, the authors remind readers of the existence of this complication. The exact cause of hyperperfusion syndrome remains unknown, however, and the treatment of hyperperfusion syndrome has not been defined.

Frank Hsu Robert F. Spetzler Phoenix, Arizona Sundt TM Jr, Sharbrough FW, Piepgras DG, Kearns TP, Messick JM Jr, O'Fallon WM: Correlation of cerebral blood flow and electroencephalographic changes during carotid endarterectomy: With results of surgery and hemodynamics of cerebral ischemia. Mayo Clin Proc 56:533–543, 1981.

The authors describe their experience with seven patients who developed cerebral hyperperfusion syndrome after undergoing treatment of severe internal carotid artery stenosis with either carotid endarterectomy or angioplasty and stenting. A detailed account of the postoperative neurological symptoms and radiographic findings is presented. On the basis of the radiographic findings, the authors define three distinct groups of hyperperfusion presentations: acute focal edema, acute hemorrhage, and delayed classic. They conclude that the syndrome of hyperperfusion may represent a number of different pathophysiological processes.

Hyperperfusion is a significant complication after carotid revascularization. Although presumedly due to increased perfusion in a maximally dilated vascular bed, the pathophysiology of hyperperfusion is not entirely clear. Although the authors do not offer any new hypotheses regarding possible pathophysiological mechanisms, their characterization of the varied clinical presentations is well documented, clear, and informative. Yet, we interpret the data otherwise-that these clinical conditions are variations of the same process whose presentation and radiological features may be dependent on the degree of severity of the hemispheric ischemia, the duration of the vasodilated state, and the levels of blood pressure and flow reaching the dilated vascular bed after the obstruction has been corrected. A carefully controlled study that includes both pre- and posttreatment cerebral blood flow measurements could clarify the risk of developing the condition and could direct the degree and duration of treatment. This additional information would allow the treating physician to differentiate hyperperfusion deficits from those that are related to intraoperative hypoperfusion.

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This article describes a retrospective review of the incidence of hyperperfusion syndrome in a series of patients who underwent surgical and endovascular treatment for internal carotid artery stenosis. The authors identified 4 (3.1%) in a consecutive series of 129 patients who underwent carotid endarterectomy and 3 (6.8%) in a consecutive series of 44 patients who underwent endovascular stenting who developed postoperative nonthrombotic neurological deficits. Although hyperperfusion syndrome was originally described as new onset of headache, seizure activity, or intracerebral hemorrhage after carotid endarterectomy, the authors propose a novel classification scheme using certain MRI and perfusion-weighted imaging parameters. Specifically, three forms of hyperperfusion syndrome are outlined on the basis of patient presenta-

Sundt TM Jr, Sharbrough FW, Piepgras DG, Kearns TP, Messick JM Jr, O'Fallon WM: Correlation of cerebral blood flow and electroencephalographic changes during carotid endarterectomy: With results of surgery and hemodynamics of cerebral ischemia. Mayo Clin Proc 56:533–543, 1981.

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tions in this series: acute focal edema, acute intracerebral hemorrhage, and 3) delayed onset (more than 24 hours) of seizures, focal weakness, or intracerebral hemorrhage.

The authors propose a clinically relevant classification system for hyperperfusion syndrome that can be diagnosed quickly with the use of new imaging procedures. This may allow for earlier and better treatment of this condition. However, the retrospective nature of this study limits significant conclusions regarding the cause of the deficits that the patients in this series sustained. Although clamp time was not found to be a statistically significant factor, the authors did not use a control group to investigate further other important factors, such as the severity of carotid stenosis, the degree of collateral supply, perioperative blood pressure as a function of baseline blood pressure, and the severity and temporal relationship of preprocedural strokes. In addition, the class and duration of antiplatelet or anticoagulant therapy were not evaluated with respect to the intracerebral hemorrhages that occurred in this series. The authors also were unable to evaluate all patients on the basis of the appropriate radiological investigations outlined in their definition. Only two of the seven patients in this series underwent diffusion-weighted MRI to rule out thromboembolic causes, and one patient underwent perfusionweighted imaging to confirm hyperperfusion of the affected hemisphere.

Despite these limitations of the study, the authors' initial work is valuable, especially with regard to the inclusion of patients who underwent endovascular carotid revascularization. Further study with the use of matched controls is required to define more precisely the incidence, pathophysiology, and prevention of this rare but important syndrome.

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Medical treatment of military wounds in World War I. Henry Tonks' An Advanced Dressing-station in France, 1918. Tonks, a medical doctor and medical educator, joined the Royal Army Medical Corps at the outbreak of World War I. During this time, he became a pioneer in the field of plastic surgery. After becoming Principal of the Slade Art School in 1917, he was appointed in 1918 as an official war artist. (Oil on canvas, courtesy of Imperial War Museum, London.)