Frequency and Pathogenesis of Hemodynamic Stroke

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Background and Purpose Hemodynamic stroke is a recognized but poorly described entity. The aim of this study was to define the frequency and pathogenic mechanisms of hemodynamic stroke.

Methods We prospectively studied 300 consecutive patients with acute ischemic stroke for evidence of a hemodynamic mechanism. All patients with a probable or possible thromboembolic source were excluded.

Results Twenty-nine patients (9.6%) had documented or presumed hypotension at stroke onset, with 27 of 29 (93%) having watershed infarction on computed tomography (CT). Most (21/29) patients had a slow (hours to days) progressive onset of stroke. Myocardial infarction, cardiac arrhythmias, and orthostatic changes in blood pressure related to diabetic dysautonomia and antihypertensive therapy were the predominant causes of hypotension. Ten patients had moderate or severe carotid stenosis (frequently bilateral); 9 had carotid occlusion (19/29 [66%]). Patients with normal carotid arteries (10/29 [34%]) had hypotension with a stuttering onset to stroke and watershed infarction on CT. Many patients continued to have progressive neurological deterioration, often with ongoing hemodynamic instability. Of 7 patients who underwent carotid endarterectomy had further perioperative ischemic events. Five patients had myocardial infarction, and overall 4 died during 18.4 months of follow-up (mortality, 9%/y).

Conclusions Recognition of the clinical and CT features of hemodynamic stroke allows early identification and management of cardiac and carotid disease and correction of iatrogenic causes of hypotension, which may reduce the risk of further events. (Stroke. 1994;25:2179-2182.)

Key Words: • carotid artery diseases • cerebral infarction • heart disease

The concept of hemodynamic disturbances of cerebral perfusion as a primary cause of stroke is not new. In the 1950s Denny-Brown1 referred to "cerebral hemodynamic crises" with focal cerebral symptoms due to an arterial stenosis or occlusion causing a state of episodic insufficiency of flow in the circle of Willis. Collateral flow was said to be the first affected by a generalized lowering of blood pressure. Many of Denny-Brown's statements are even more relevant today, particularly the prophetic warnings regarding the need to avoid excessive use of antihypertensive drugs and maintain an adequate blood pressure in acute stroke.3 Although the majority of cerebral ischemic events are thromboembolic,4,7 recognition of a hemodynamic subgroup5,8 has important implications for investigation and management. Estimates of frequency range from 8% to 53% of ischemic stroke.9,10 Causes of stroke due to cerebral hyperperfusion include orthostatic hypotension (due to diabetic dysautonomia or antihypertensive therapy),2,4,11-13 orthostatic cerebral ischemia (without hypotension),14-16 perioperative complications (especially cardiac surgery),3,17,18 myocardial ischemia,9,11,19,20 cardiac arrhythmias,11,19,21 severe carotid stenosis or occlusion,2,11,19,22,23 or frequently combinations of these.

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or arterioembolic stroke (diagnosed after the clinical and laboratory workup) were excluded from the study.

All stroke unit patients routinely have an electrocardiogram, full blood count, glucose, urea and electrolyte analysis, CT, transcranial Doppler (TCD), and carotid duplex ultrasonography. Patients are monitored for postural hypotension. Investigations such as digital subtraction angiography, echocardiography, and Holter monitor are performed as clinically indicated.

Patients were considered as having had a possible hemodynamic stroke based on one or both of the following criteria: (1) documented or presumed hypotension at stroke onset or (2) CT evidence of watershed infarction.

If, however, after careful consideration, an embolic source could not be ruled out as the primary cause of stroke, the patient was excluded from analysis.

Carotid stenosis was defined as the percent diameter reduction of the internal carotid artery (ICA), according to previously published angiographic and duplex criteria. TCD collateral cerebral blood flow patterns that were considered indicative of compromised cerebral perfusion were the absence or reversal of flow through the components of the circle of Willis or ophthalmic arteries.

All CT scans were reviewed by a neuroradiologist. Infarcts were defined using the charts of Damasio and previously used criteria for watershed infarction.

Risk factor prevalences in patients with hemodynamic stroke were compared with those in patients without hemodynamic stroke for the same period by $\chi^2$ analysis. The mean follow-up was 18.4 months.

**Results**

Twenty-nine patients (9.6%) were identified with hemodynamic stroke, of whom 27 had watershed infarction and 2 pial territory infarcts.

**Documented or Presumed Hypotension**

Cardiac disorders (bradyarrhythmias and tachyarrhythmias, myocardial ischemia) and orthostatic hypotension (usually due to diabetes or antihypertensive therapy) were prominent among 15 patients with documented hypotension and 14 additional patients in whom hypotension was strongly suspected on the basis of syncope or near syncope at the time of stroke (Table). In many patients the cause of hypotension was multifactorial, eg, syncope in a patient with carotid stenosis, complicated diabetes, and multiple antihypertensive agents. The majority of patients (21/29) had a progressive onset to stroke (hours to days), often with stereotyped responses to repeated episodes of hypotension. No patients had atrial fibrillation or a thromboembolic source found with echocardiography. In some cases symptomatic arrhythmias were paroxysmal and only detected by repeated 24-hour Holter monitoring. Nine patients had carotid occlusion (all with contralateral carotid disease), and 20 had moderate (50% to 75%) or severe (>75%) carotid stenosis, with abnormal collateral flow patterns on TCD. Patients with a normal carotid duplex ultrasound (10/29) had a stuttering onset with recurrent episodes of hypotension and watershed infarction (frequently bilateral) on CT, including 2 diabetic patients who experienced syncope and stroke during severe vomiting.

Two patients with bilateral ICA stenosis/occlusion greater than 90%, abnormal collateral flow (and no embolic occlusion) on TCD, and recurrent witnessed syncopal transient ischemic attacks with hemiparesis had small pial territory infarcts on CT. Despite the possible embolic cause of infarction (see "Discussion"), it was believed that the primary cause of stroke was nevertheless hemodynamic, and these patients were included.

**Watershed Infarction**

Twenty-seven patients (93%) had watershed infarction. Thirteen infarcts involved the internal border zone between superficial and deep arterial perforators, 8 the posterior border zone between middle cerebral and posterior cerebral arterial territories, and 5 the anterior border zone between the middle and anterior cerebral arteries. One patient had infarction in the cerebellar border zone between superior and anterior inferior cerebellar arteries. The finding of internal watershed infarction on CT was strongly correlated with severe carotid disease and hypotensive events and is the subject of a separate publication.

**Risk Factors**

Comparison of risk factor prevalences in patients with and without hemodynamic stroke revealed significant differences for cardiac disease ($P<.005$) and carotid disease (severe carotid stenosis/occlusion; $P<.0001$) but not for smoking or diabetes.

**Outcome**

Seven patients experienced later recurrence or worsening of neurological deficit. During follow-up 5 patients had myocardial infarction. Seven patients underwent carotid endarterectomy by experienced vascular surgeons, of whom 3 experienced a worsening or recurrence of their neurological deficit in the perioperative period. Ongoing hypotension (often with associated limb shaking) was seen in 5 patients (17%), of whom 2
went on to further stroke. Four patients died (1 stroke, 1 cancer, 1 renal failure, 1 cardiac) during follow-up, for a death rate of 9%/y.

Discussion

The results of this study reveal that hemodynamic stroke may be more frequent than previously realized, accounting for 9.6% of stroke unit admissions. This is similar to previous estimates (7.7%), although hospital and autopsy studies suggest that this could be a considerable underestimate.9,10

The criteria we used encompass not only those patients with documented hypotension at stroke onset but also those in whom the clinical and CT features indicate hemodynamic impairment of cerebral blood flow, rather than emboli, as the primary cause of stroke. All patients (except two) had evidence of hypotension and watershed infarction, commonly in association with severe carotid stenosis/occlusion. Accordingly, cardiac disease and carotid disease were the most prominent risk factors. As shown in this study, a hemodynamic stroke typically exhibits a slowly progressive or stuttering course over several hours to days.22 In contrast, embolic stroke is usually of sudden onset, with the neurological deficit maximal at or near the time of the event.7,26,37 Transcranial Doppler revealed the absence of vessel occlusion and patterns of collateral flow through the circle of Willis associated with reduced cerebral perfusion pressure.30,38 Although an embolic cause of stroke cannot be completely excluded, these clinical and CT features make it unlikely, particularly in the absence of thrombus on echocardiography. For the purposes of this study we excluded doubtful cases, but it is still quite possible that patients with unobserved collapse (with or without carotid stenosis) and watershed infarction may also have had a hemodynamic stroke.

The high frequency of hemodynamic stroke may in part be explained by our stroke population being older than in other studies.7,29 Shuaib and Hachinski13 found watershed infarction to be more common in the elderly, largely attributable to hemodynamic disturbances such as postural hypotension, cardiac arrhythmias, and overzealous use of antihypertensive drugs. Orthostatic hypotension occurs in 14% to 33% of persons aged older than 60 years, with the degree of postural fall varying with activity, hydration, and timing of meals and medication.4 It has been identified as a significant risk factor for stroke in a number of prospective population-based studies.40-42

Two patients with bilateral severe carotid disease had hypotension (recurrent syncope) in association with pial territory infarction. The precise nature of infarction in these patients is unclear; although presumably embolic in origin, hemodynamic features were prominent before and at the onset of stroke. The sequence of events may therefore be an acute reduction of perfusion pressure in an already hemodynamically compromised stenosis, leading to thrombus formation, which then detaches into the middle cerebral artery and pial vessels.22

Watershed infarction is not adequately explained by embolic phenomena. Ringelstein et al22 used TCD and angiography to examine 44 patients with carotid occlusion and watershed infarction and failed to reveal any evidence of secondary emboli to explain the CT findings; furthermore, no cases of watershed infarction were found among 60 consecutive cases of proven cardioembolic stroke.64 Hemodynamic dysfunction was therefore proposed as the principal cause of this form of stroke. This is further supported by recent serial magnetic resonance imaging studies that show the development of "low-flow" strokes in fully anticoagulated patients undergoing therapeutic occlusion of the ICA.4 Other studies have shown that patients with carotid occlusion and watershed infarction frequently have syncope or near syncope at stroke onset.11,22,23

Watershed infarction occurred most frequently in the corona radiata (or centrum semiovale43) and has been described in up to 40% of patients with symptomatic carotid artery disease.19,22,24,46 Positron emission tomography and single-photon emission computed tomography studies have demonstrated that these white matter infarcts have reduced regional cerebral blood flow, reduced perfusion reserve (regional cerebral blood flow/regional cerebral blood volume), and an elevated regional oxygen extraction fraction, indicative of a hemodynamic origin.24,47,49 These blood flow imaging techniques may help in the differentiation between watershed infarction and deep lacunes (in the basal ganglia/internal capsule) or striatocapsular infarcts,50 which have a different pathogenesis and outcome and preserved cerebral perfusion reserve.34

In general, hemodynamic stroke is indicative of a poor prognosis. The mortality rate of 9%/y is comparable to that in previous studies (10%/y), and there is a high incidence of myocardial infarction and recurrent or progressive stroke. Indeed, patients with hemodynamic stroke exhibit most of the recently published key prognostic risk factors for repeated stroke (male, aged >65 years, recurrent attacks, ischemic heart disease/myocardial infarction, watershed infarction on CT).25 Care should be taken when performing interventional procedures such as carotid endarterectomy or the treatment of acute hypertension so that cerebral perfusion is maintained.

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References


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