Cerebral Blood Flow and Neurological Change in Chronic Heart Failure

Robert H. Ackerman, MD, PhD

In their article in this issue of Stroke, Gruhn et al report that cerebral blood flow (CBF) is reduced about 30% in patients with NYHA III/IV heart failure but has normalized when retested in 5 subjects 30 days after successful heart transplantation. The authors suggest that (1) the reduced CBF found before transplantation is responsible for neurological signs and symptoms reported in patients with chronic heart failure (CHF), and (2) that the resolution of such symptoms after transplantation, as reported in other studies, and the normalization of CBF, as found in their investigation, are parallel phenomena, both resulting from an improvement in central hemodynamics.

This editorial explores whether the increase in CBF 30 days after transplantation found by Gruhn et al could be on another basis—a perisurgical fall in hematocrit—and whether the reduced CBF values found before surgery are sufficient to cause neurological disturbances. It also considers the types and etiologies of neurological changes in CHF.

Hematocrit and CBF Relationships

Hematocrit is the main determinant both of whole-blood viscosity and arterial O$_2$ content, each of which has powerful effects on CBF. Viscosity accounts for 56% of the decrease in CBF that occurs as hematocrit rises from 20% to 40%. In dilated cardiomyopathy, viscosity is further increased due to elevated fibrinogen and decreased red cell deformability, which can compound the inverse effect of hematocrit on CBF. A reduction in arterial oxygen content can account for 40% to 60% of the increase in CBF that accompanies a fall in hematocrit. A drop in hematocrit can occur perisurgically from blood loss or relative hemodilution.

Some years ago we noted (data reported at meetings but unpublished) that paired CBF measurements, done shortly before and after unilateral carotid endarterectomy (CEA) in patients with single-vessel disease, showed a statistically significant postoperative increase in CBF (>15%) in only 9 of 33 subjects studied. However, in these 9 the increase was bilateral. The bilateral nature of the response could not be explained by clinical, blood gas, or vascular pathoanatomic findings. Because of a focus on CBF/viscosity relationships at the time, we were able to examine correlative data on hematocrit and fibrinogen.

We found a significant postoperative percentage fall in hematocrit in the 9 patients in whom CBF rose significantly compared with the 24 in whom it did not (Table). The between-group differences in percent change in CBF and hematocrit, before versus after CEA, were significant at $P<0.001$ and $P<0.005$, respectively (1-tailed t test). The fibrinogen changes were not significant.

We concluded that the global CBF rise in the 9 patients resulted primarily from rheological rather than hemodynamic changes and that the rheological changes were most directly related to the significant fall in hematocrit.

Few published reports provide quantitative bilateral CBF data within weeks before and after CEA. Only 1 such communication that we have identified, by Schroeder et al, gives hematocrit or hemoglobin data. In 32 subjects, these authors found a global CBF rise of about 35% and a coincident mean hemoglobin drop of about 7% on the first day after CEA. Over the next week, the initially observed bilateral CBF increase declined toward preoperative levels, based on studies done at 2 to 4 and 5 to 11 days postoperatively. (It is not clear from the report how the patients examined at day 1 overlapped with those studied during the later intervals.) The authors postulated that “hemodilution” may have accounted for the initial bilateral global flow increase. They did not find a direct correlation between the decrease in hemoglobin and the increase in CBF, nor did they present hematocrit data.

Gruhn et al do not provide data on hematocrit before or after cardiac transplantation. For the purposes of this editorial, we reviewed hematocrit data on 10 recent consecutive cardiac transplantation cases at the Massachusetts General Hospital. In 7 patients hematocrit values before transplant were significantly higher than at 30 days after transplant ($P=0.026$). The mean hematocrit value for the 7 fell from 36.3±7.7 to 29.6±6.1, which represents an 18.5% fall. In the other 3 patients, the mean hematocrit value rose from 31.8±3.31 to 35.6±1.61, an increase of 11.9%. The net hematocrit change for all 10 patients was −8.30%.

Based on the aggregate observations above, one may reasonably suggest that a lower mean hematocrit value could have accounted in part or in full for the increase in mean CBF found by Gruhn et al in their 5 cases studied 30 days after transplantation.

Similar rheological considerations theoretically could underlie the differences in the CBF response to captopril reported in back-to-back articles in the American Journal of Medicine in 1984, one of which is cited by Gruhn et al. Patients in both investigations had NYHA class III/IV heart failure. In the cited report, Rajagopalan et al did baseline and postcaptopril CBF studies on 9 hospitalized subjects who received increasing captopril doses over 48 to 72 hours. CBF studies performed after the completion of the captopril regimen showed a 21% increase.
in CBF. In the study by Paulson et al., the investigators measured CBF in 5 outpatient subjects at baseline and 15, 60, and 180 minutes after captopril administration. CBF remained stable at each of the 4 study points.

In a published discussion of the 2 papers, Paulson sought an explanation for the discrepancy in the CBF findings between the inpatient and outpatient studies, adding that his group had found no change in CBF even after 1 to 3 weeks of outpatient captopril treatment. He queried whether the difference in the CBF results might have something to do with hospitalization itself and alluded to a report of increased CBF in severely demented patients “after they had received good hospital care for one or two weeks with no specific medical treatment.” Inhospital patients can demonstrate a drop in hematocrit, which can alter CBF, on the basis of daily blood drawing and/or increased hydration. The hydration can result from intravenously administered fluids or increased oral consumption with medications.

Consideration of the potential impact of hematocrit change on CBF in diverse clinical and research situations is important, as it underscores the fact that unless correlative hematocrit information is available, one is at risk of misapplying CBF findings due to an underscoring of the fact that unless correlative hematocrit information is available, one is at risk of misapplying CBF findings due to an

### Percent Change in CBF and Whole-Blood Viscosity Factors Before and After CEA

<table>
<thead>
<tr>
<th>CBF % Δ Pre-/Post-CEA</th>
<th>n</th>
<th>CBF % Δ Pre-/Post-CEA</th>
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<tbody>
<tr>
<td>15%</td>
<td>9</td>
<td>25±15*</td>
</tr>
<tr>
<td>NS</td>
<td>24</td>
<td>5±13</td>
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</tbody>
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*Hct indicates hematocrit; NS, not significant. CBF values are milliliters per 100 g per minute.

### Types of Neurological Deficits in CHF Patients

In a recent review covering the period 1966–2000, Almeida and Flicker found 13 studies that examined the association between congestive heart failure and cognitive, including several done on heart transplant candidates. Commenting on “the enormous paucity of systematic information,” they identified only 5 investigations which, in their opinion, were “suitable for analysis.” Pooled data from these 5 studies suggested an association between congestive heart failure and generalized cognitive impairment, including attention and memory deficits.

How the patients are selected and tested affects the range of deficits detected. In a study before and after cardiac transplantation in patients who were not screened for comorbidities, Schall et al. found impairments in memory, abstract reasoning, and tactual perceptual processing deficits. In a study that excluded subjects with other medical and neurological problems, more limited cognitive deficits were identified. Roman et al. using a battery of 10 neuropsychological tests on 17 patients before cardiac transplantation who had no prior history of stroke, anoxic events, renal failure, or other medical illness, found definite abnormalities only in delayed recall (Rey Auditory Verbal Learning Test and Bender-Gestalt Test). Tests of diffuse cerebral dysfunction, such as sustained concentration and graphomotor learning, were all normal before transplantation.

Changes in cognitive functioning after cardiac transplantation have been reported as follows: 1 year following transplant, 14 of 16 patients studied by Roman et al. who had an abnormal Rey Auditory Verbal Learning Test before transplant showed normal results after transplant; however, the Bender Gestalt Test findings showed only a slight improvement that was of “dubious clinical significance.” The study had no control group. In the series of Schall et al., the only significant improvement 4 to 11 months after cardiac transplant was in motor speed. Augustine et al. examined 10 patients before and 1 month after cardiac transplant. Seventy percent showed a decline on delayed recall testing. Whether the poorer outcome in these patients reflects preexisting permanent cerebral damage or secondary periprocedural injury is uncertain. Although death and stroke are uncommon events now in cardiopulmonary bypass surgery, in some reports up to two thirds of patients show new evidence of neuropsychological dysfunction postoperatively.

### Causes of Neurological Deficits in CHF Patients

Roman et al. attributed isolated memory impairments to hypoperfusion in mesial temporal lobe structures. However, as

*100 g·min⁻¹, 10 Baron cites PET studies in patients with acute stroke in which the highest CBF for penumbral tissue that evolved to infarction was 17 to 22 mL·100 g⁻¹·min⁻¹.*

These studies do not necessarily relate to the CBF threshold required to produce clinical cognitive dysfunction, but they support the impression that the brain is more tolerant of oligemia than early investigators had anticipated.
documented pathologically by Brierley and Miller in 1966,18 the hippocampus should not be involved in cerebral low-flow “watershed” ischemic events, whereas the hippocampus is highly susceptible to hypoxic injury.

Gruhn et al speculate that the neurological impairments reported by other authors could result from a combination of reduced mean arterial blood pressure, exhausted cerebrovascular reserve, and/or failure of systemic mechanisms for redistributing cardiac output to the brain. As indicated in their discussion, little is known about cerebral vasoregulation in severe CHF, including whether autoregulation remains intact and, if so, if the lower limits of autoregulation have shifted up due to preexisting hypertension, down due to intervening chronic hypotension or have been modified by the actions of certain types of drugs such as angiotensin-converting enzyme (ACE) inhibitors. Vasoregulatory responses may persist but reserve may be exhausted, as suggested by the study of Georgiadis et al.19 In extreme pathophysiological circumstances such as cardiogenic shock and subarachnoid hemorrhage, an increase in cardiac output with intraaortic balloon pumping may cause an increase in CBF independent of arterial blood pressure.20,21

Except in patients with underlying cerebrovascular obstructive disease or prior stroke, lateralizing or focal sensorimotor changes seem to be uncommon in patients with CHF. Although cognitive deficits may increase with CHF severity (diminished ejection fraction, cardiac output, and/or cardiac index),22–24 they may better reflect the effects of generalized disturbances in systemic and brain homeostatic mechanisms, triggered by CHF, and often are superimposed on organ functions already compromised by diabetes, hypertension, and atherosclerosis. Impaired attention and memory difficulties are nonspecific findings that potentially could occur with or be complicated by severe hypoperfusion. However, they may be more common with hypoxic/toxic/metabolic disturbances and, as Almeida and Flicker13 point out, depression. Of course, the failing heart is thrombogenic, and one cannot exclude showers of cerebral microemboli that may cause diffuse gray matter injury. Such microemboli can be detected with transcranial Doppler studies, as has been shown by monitoring during cardiopulmonary bypass procedures.17

The fact is that the causes of the neurological deficits in patients with CHF are not known. Good evidence is wanting at present that the neurological changes in CHF are on the basis of brain hypoperfusion or that a cognitive improvement following cardiac transplant may be demonstrated by the actions of certain types of drugs such as angiotensin-converting enzyme (ACE) inhibitors. Vasoregulatory responses may persist but reserve may be exhausted, as suggested by the study of Georgiadis et al.19 In extreme pathophysiological circumstances such as cardiogenic shock and subarachnoid hemorrhage, an increase in cardiac output with intraaortic balloon pumping may cause an increase in CBF independent of arterial blood pressure.20,21

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References


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