There was a significant relationship between plasma glucose and the volume of the intracerebral lesion volume as measured on computed tomographic scan \((r=0.469, P=0.001)\), but a stronger relationship was observed between serum cortisol and lesion volume \((r=0.542, P<0.001)\). Neither hemoglobin A1 nor plasma noradrenaline levels were significantly correlated with lesion volume.

Fasting plasma glucose was measured in survivors over the course of the study. There was a significant decrease in the fasting glucose levels on the order of 1 mmol/L over the first 7 days after stroke onset. This is in keeping with the results of Melamed,\(^3\) who found that hyperglycemia after stroke returned to normal levels a mean of 3.5 days after stroke. Hyperglycemia after stroke fulfills the criteria for stress hyperglycemia, ie, it is elevated in proportion to the severity of the illness, it is related to the mediators of the stress response, and it is a temporary phenomenon.

van Kooten and colleagues were not able to demonstrate this phenomenon because they measured only catecholamines. While catecholamines are related to injury,\(^4\) they are extremely sensitive to stress. Admission to a hospital is a stressful event, and this “background noise” may have obscured the relationship between glycaemia and catecholamines. Even though we attempted to standardize the stress as much as possible, other factors known to alter plasma catecholamine levels,\(^5\) such as caffeine intake, sodium intake, cardiac output, and renal clearance of catecholamines, were not controlled in either study. The estimation of picogram quantities of adrenaline and noradrenaline is technically difficult. The plasma half-life of these substances is quite short, and a “background noise” may have obscured the relationship between glycaemia and catecholamines. Even though we attempted to standardize the stress as much as possible, other factors known to alter plasma catecholamine levels,\(^5\) such as caffeine intake, sodium intake, cardiac output, and renal clearance of catecholamines, were not controlled in either study. The estimation of picogram quantities of adrenaline and noradrenaline is technically difficult. The plasma half-life of these substances is quite short, and a proportion of the noradrenaline or the majority of the adrenaline response may have decayed even before the first sample in the van Kooten study was taken, as the flow phase of the stress response is established after 24 hours.\(^4\)

In short, we agree with the findings of van Kooten et al, but we cannot agree with their conclusion that hyperglycemia after stroke is not due to a stress response. We believe that there is evidence that there is a stress hyperglycemic response in the early stages of acute stroke. The nature of the stress response, and in particular the influences of central centers in the brain on the response, has yet to be elucidated.

**References**


**Response**

We thank Drs Tracey and Stout for their comments on our study. In accordance with our results, these authors have found no association between plasma norepinephrine and blood glucose in patients with acute ischemic stroke. However, as they point out, there are two main differences between their findings and ours: (1) they have found a relationship between cortisol—which we did not measure—and glucose levels and (2) in hyperglycemic patients who were not known to have diabetes, glucose levels dropped consistently after the acute period. Drs Tracey and Stout regard these findings as convincing evidence that hyperglycemia was caused by stress in these patients.

However, as the authors themselves state, norepinephrine and epinephrine are much more sensitive to stress than cortisol.\(^1\) Several studies in humans indicate that circulating norepinephrine and epinephrine, administered exogenously and leading to high physiological concentrations, do not alter plasma corticotropic and cortisol.\(^2,3\) Furthermore, although Tracey and colleagues found a significant correlation between cortisol and glucose, the strength of the relationship was modest \((r=0.25)\). Moreover, elevation of cortisol only, without a concomitant rise in epinephrine and glucagon, would not be expected to cause hyperglycemia in the acute phase.\(^4\)

We have checked the glucose levels after 2 weeks in our patients with latent diabetes and in those with idiopathic hyperglycemia. Patients with latent diabetes had similar values during the acute stage and after 2 weeks. In agreement with Tracey and colleagues, patients with idiopathic hyperglycemia showed a decrease in the mean glucose level of 1.1 mmol/L. However, 67% of these patients still had an elevated (ie, >6.7 mmol/L) blood glucose after 2 weeks. Furthermore, normalization of the blood glucose after the acute stage in some patients does not exclude the possibility that factors other than stress (eg, increased insulin resistance) may have caused temporary hyperglycemia. Also, sustained elevation of blood glucose after the acute phase may be caused by increased insulin resistance, independently of epinephrine, glucagon, and cortisol levels.\(^1\) However, the insulin clamp technique, which was not used in either study, is mandatory to obtain reliable data on insulin resistance.\(^1,6\)

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**Nailfold Capillary Microscopy in Lacunar Infarction**

Nailfold capillary microscopy is a useful, noninvasive procedure that allows the direct observation of in vivo microvascular abnormalities in the skin.\(^1,2\) Various capillaroscopy abnormalities have been described in different cardiovascular, endocrine, rheumatic, and neuropsychiatric diseases.\(^3\) A constant typical capillaroscopic pattern, generally characterized by a diffuse microangiopathy, has been described in a few diseases. In particular, in systemic sclerosis (scleroderma), nailfold capillary microscopy shows a characteristic pattern that includes loss of capillaries, tortuous and enlarged capillary loops, and bushy loops.\(^1,3\) In neuropsychiatric diseases, capillaroscopy revealed some capillary abnormalities; however,
the data reported in the literature are generally contrasting and not conclusive.2 The aim of our study was to investigate the presence of capillaroscopic alterations in patients with lacunar infarctions (LIs). The LIs are small infarcts that occur in the subcortical regions of the brain (ie, deep white matter, basal ganglia, internal capsule, thalamus, and brain stem), with consequent variable clinical syndromes.4 Pathological lesions underlying the lacunes are small-vessel lipohyalinosis or microatheroma, while arterial hypertension and diabetes mellitus are the most frequent risk factors.4-6 Twenty consecutive patients followed up at the Neurology Institute of the University of Pisa (14 men and 6 women, mean±SD age 68±7 [range, 55 to 78] years) with LI and without other neuropsychiatric disorders were studied. In addition, two other age- and sex-matched groups were included in the study as controls: 20 patients with cortical or subcortical cerebral infarction and 20 healthy control subjects. Patients with LI had motor, sensory, or sensorimotor stroke; in all cases, diagnosis of LI was based on computed tomographic scan results. A clinical assessment was carried out in all LI and control groups and included epidemiological, medical, and neurological history; physical examination; and laboratory results. In addition, carotid flow was evaluated by Doppler analysis. Various risk factors (arterial hypertension, diabetes mellitus, carotid stenosis, coronary insufficiency, smoking, altered lipid metabolism) were recorded with variable but not significantly different frequency in both LI patients and control groups. Capillaroscopic examinations were performed by the same investigator (C.F.), blinded to the protocol, using a Leitz stereomicroscope at 12× magnification, as previously described.5,6 All digits of both hands, excluding the thumbs, were examined. The Table summarizes the capillaroscopic alterations found in LI patients and control groups.

Tortuous capillary loops and other minor morphological abnormalities were recorded with comparable frequency in both LI patients and control subjects. On the contrary, in the large majority of LI patients the subpapillary venous plexus was clearly evident in at least half of the digits examined; the prevalence of this finding resulted in statistical significance when compared with cerebral infarction patients and healthy control subjects (P<.001).

In our present series of patients with LI, the almost-constant presence of capillaroscopic alterations in patients with lacunar infarction patients; and SVP, subpapillary venous plexus.

<table>
<thead>
<tr>
<th>Finding</th>
<th>LI, %</th>
<th>CI, %</th>
<th>Control, %</th>
<th>χ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tortuous loops</td>
<td>25</td>
<td>20</td>
<td>25</td>
<td>NS</td>
</tr>
<tr>
<td>Loss of capillaries</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Enlarged loops</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>SVP visibility</td>
<td>90</td>
<td>15</td>
<td>10</td>
<td>P&lt;.001</td>
</tr>
</tbody>
</table>

LI indicates lacunar infarction patients; CI, cerebral infarction patients; and SVP, subpapillary venous plexus.

References
Nailfold capillary microscopy in lacunar infarction.
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