Carbon dioxide reactivity and patterns of cerebral infarction in patients with carotid artery occlusion

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Summary. A total of 106 patients with 112 internal carotid artery occlusions were investigated by cranial computed tomography and transcranial Doppler ultrasonography (CO₂ test), giving a measure of the cerebrovascular reserve capacity. The morphological patterns of the ischaemic lesions were classified into three categories: lacunar, thromboembolic and haemodynamic infarctions. Of 29 patients with an exhausted CO₂ reactivity, 19 showed a haemodynamic type of infarction, whereas of 45 cases with a normal CO₂ reactivity only 2, and of 38 patients with a diminished CO₂ reactivity only 3 had haemodynamically caused infarctions (P < 0.001). The correlation between an exhausted CO₂ reactivity and the presence of haemodynamic infarctions could be of value for therapy in patients with carotid artery occlusions.

Key words: Transcranial Doppler ultrasonography - Vascular reactivity - Cranial computed tomography - Cerebral ischaemia

Patients and methods

A total of 131 patients with 122 unilateral and 9 bilateral ICA occlusions were included in the study. MCA blood flow velocity and end-tidal PCO₂ were monitored during steady states of normocapnia, hypercapnia induced by breathing a mixture of 5% CO₂ in 95% O₂, and hypocapnia due to voluntary hyperventilation. Normally the relationship of the cerebral blood flow velocity to the concentration of CO₂ in the blood shows a sigmoid curve with a linear relation in the physiological range between 30 and 50 mmHg PCO₂. In pathological cases the curve is shifted to the left, resulting in a decreased flow during hypercapnia or even the absence of a response to hyper- as well as to hypocapnia (Fig. 1). Based on previous validation studies three categories of sufficient, decreased and exhausted CO₂ reactivity were distinguished [11] (Table 1).

In patients with a sufficient CO₂ reactivity, the MCA blood flow velocity increases at least 10% during hypercapnia of 1 vol% enhancement of end-expiratory CO₂ and decreases at least 10% during hypocapnia of 1 vol% diminution of CO₂ as compared with the physiological base line. A decreased reserve capacity is characterized by a markedly diminished or complete lack of increase in flow during hypercapnia. An exhausted CO₂ reactivity is defined...
in 6 (13%) cases; only 2 (4%) showed haemodynamic lesions ipsilateral to the ICA occlusion (Fig. 2).

Of the 45 patients with a normal CO2 reactivity, there were 21 (47%) with a thromboembolic type of infarction and 16 (36%) with no lesions. Microangiopathy was found in 5 (11%) cases; only 2 (4%) showed haemodynamic infarctions. In the group with a diminished CO2 reactivity (n = 38), 16 (42%) had no brain lesions, 12 (32%) revealed thromboembolic infarctions, 7 (18%) showed microangiopathic changes and only 3 (8%) had haemodynamic lesions.

In contrast to the first two groups, the patients with an exhausted CO2 reactivity (n = 29) showed a completely different distribution of ischaemic patterns. Almost two-thirds of the patients were found to have haemodynamic lesions ipsilateral to the ICA occlusion: 19 (66%) had a terminal zone or watershed infarction, whereas a territorial ischaemia was present in only 5 (17%) cases; another 5 (17%) had no cerebral lesions (Fig. 1). The difference between the patients with an exhausted CO2 reactivity and those with a normal or diminished cerebrovascular reserve capacity was highly significant (chi square test, P < 0.001).

**Discussion**

The comparison between CO2 reactivity and patterns of infarctions in cranial CT revealed a highly significant correlation between a lack of cerebrovascular reserve capacity and haemodynamically caused ischaemia. These findings support earlier published investigations concerning the relationship between clinical symptoms and CO2 reactivity. When investigating patients with subtotal ICA stenoses and occlusions, recent ipsilateral ischaemic events have been found to occur more often in patients with a pathological Doppler CO2 result than in those with a sufficient cerebrovascular reserve capacity [10, 12].

In patients with ICA occlusions, Ringelstein et al. [6] and Ringelstein and Weiller [4] also found an association of haemodynamically caused lesions and ipsilateral clinical symptoms with reduced CO2 reactivity. In 16 patients with low-flow infarctions, the mean autoregulatory reserve was significantly lower than in 20 patients with normal CT scans and in 28 patients with thromboembolic lesions. There was no significant difference between subjects with territorial infarctions and those with normal CT scans.

In our studies the extent of structural damage in the brain did not influence CO2 reactivity, since neither embolic nor microangiopathic patients showed significant

![Fig. 1A-C. Classification of the CO2 reactivity into three groups (after Widder [11]). The three graphs show the relation of middle cerebral artery (MCA) blood flow velocity to end-tidal PCO2 in the case of normal, diminished and exhausted CO2 reactivity. A Normal, B diminished, C exhausted; □ ± 1 vol% CO2 range](image)

![Fig. 2. Ipsilateral cranial CT patterns in 112 internal carotid artery occlusions (106 patients). The cerebral infarctions are subdivided into microangiopathic, thromboembolic and haemodynamic lesions. □ Normal, □ diminished, • exhausted CO2 reactivity](image)

**Table 1. Classification of CO2 reactivity. Hyper-/hypocapnia method for the evaluation of CO2 reactivity (after Widder [11]). The three graphs show the relation of middle cerebral artery (MCA) blood flow velocity during different states of end-tidal PCO2.**

<table>
<thead>
<tr>
<th>CO2 reactivity</th>
<th>Change in MCA velocity referred to physiological baseline values</th>
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<tbody>
<tr>
<td></td>
<td>Increase during hypercapnia of + 1 vol% CO2</td>
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<tr>
<td>Normal</td>
<td>≥ 10%</td>
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<tr>
<td>Diminished</td>
<td>-</td>
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<td>Exhausted</td>
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as a complete lack or negligible change in blood flow during hyper- as well as hypocapnia.

The CT images were analysed by two investigators, who were in agreement without knowledge of the clinical data and Doppler ultrasonography findings. The patterns of the supratentorial ischaemic lesions were classified into three categories: lacunar [2, 5]; thromboembolic [14] and haemodynamic [1, 13] infarctions.

Exclusion criteria for the evaluation of the CT scans were: insufficient quality of the scans; small cerebral lesions only in one slice, especially in the subcortical region, to avoid partial volume effects; a defect of the skull, because in this case a traumatic origin of the cerebral lesion could not be excluded; CT lesions which could not be classified in one of the three categories; and CT scans with a combination of territorial and haemodynamic infarctions.

**Results**

A total of 106 patients with 112 ICA occlusions were included in the final evaluation. Twenty-five patients with 28 ICA occlusions had to be excluded: 14 CT scans fulfilled the previously defined exclusion criteria and in 14 cases the CO2 reactivity ipsilateral to the ICA occlusion could not be measured because of insufficient ultrasound transmission through the temporal bone.

Thirty-seven patients had no localized ischaemic cerebral defects. The other 69 patients investigated showed ischaemic lesions ipsilateral to the ICA occlusion (Fig. 2). Of the 45 patients with a normal CO2 reactivity, there were 21 (47%) with a thromboembolic type of infarction and 16 (36%) with no lesions. Microangiopathy was found in 6 (13%) cases; only 2 (4%) showed haemodynamic infarctions. In the group with a diminished CO2 reactivity (n = 38), 16 (42%) had no brain lesions, 12 (32%) revealed thromboembolic infarctions, 7 (18%) showed microangiopathic changes and only 3 (8%) had haemodynamic lesions.

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