

Original article

Cerebral blood flow and oxygen metabolism in symptomatic internal carotid artery occlusion by (traumatic) cervical artery dissection

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Abstract

The present study investigates whether cerebral infarction resulting from internal carotid artery occlusion by cervical dissection is due to emboli, released from a superimposed luminal thrombus, or is due to haemodynamic failure and hypoperfusion. Ten patients with a history of stroke and with a visible cerebral infarct on computed tomographic scan, due to cervical dissection and thrombosis of the internal carotid artery, were studied with positron emission tomography in order to assess the regional cerebral blood flow (rCBF), the regional cerebral metabolic rate of oxygen (rCMRO₂) and the regional oxygen extraction fraction (rOEF) in different regions of the brain. rCBF and rCMRO₂ were only decreased in the infarct area but not in the peri-infarct zone or elsewhere in the brain. As rOEF was not increased in the affected cerebral hemisphere, the present study suggests artery-to-artery embolism rather than a haemodynamic event as the cause of the stroke. Use of anticoagulants thus appears to be the appropriate treatment in the acute stage.

Key words: Positron emission tomography ; internal carotid artery occlusion ; cervical dissection ; artery-to-artery embolism ; chronic hypoperfusion ; anticoagulantia.

Introduction

In most cases of cervical dissection of the internal carotid artery a major, minor or even minimal head or neck trauma can be detected as the initial triggering event, causing a bleeding in the arterial wall and subsequent occlusion of the lumen (Stapf *et al.*, 2000). It is a rare cause of stroke, mainly affecting young individuals. The functional recovery is considered to be good in the majority of patients (Stapf *et al.*, 2000 ; Leys *et al.*, 1995 ; Touze *et al.*, 2003), although some reports mention severe persistent neurological deficits and a high mortality rate (Guillon *et al.*, 1998 ; Zetterling *et al.*, 2000). However, as the incidence of asymptomatic carotid dissection is not known, outcome measures are uncertain (Schievink *et al.*, 1994).

The annual rate of stroke recurrence is low, between 2.0 and 4.5 % (Leys *et al.*, 1995 ; Zetterling *et al.*, 2000 ; Schievink *et al.*, 1994 ; Basetti *et al.*, 1996). In severe cases more territorial than borderzone infarcts are found, suggesting artery-to-artery embolism as a more frequent cause than haemodynamic events (Basetti *et al.*, 1996 ; Lucas *et al.*, 1998). However, this matter is not settled at present.

The present positron emission tomographic (PET) study investigates cerebral blood flow and oxygen metabolism in different brain regions of patients suffering from a stroke due to internal carotid artery occlusion by cervical dissection. The aim of the study is to find out whether the cerebral infarcts are due to emboli, released from the carotid lesion, or due to global hypoperfusion resulting from the carotid artery occlusion.

Patients and methods

Ten consecutive symptomatic patients with internal carotid artery occlusion due to cervical dissection, who agreed with the PET study, were recruited during 1990 and 1999. All patients had been admitted to the Neurological Department of the Ghent University Hospital for evaluation and treatment of a first stroke. The severity of neurological impairment on admission was determined with the Orgogozo stroke scale (Orgogozo and Capildeo, 1984). In six of the ten patients a minor head or neck trauma preceded the stroke onset. All patients had a visible infarct on computed tomographic (CT) scan of the brain. The carotid occlusion was demonstrated by conventional angiography in all patients. The diagnosis of cervical dissection was retained as etiology when severe luminal narrowing (string sign) started approximately 2 cm postbifurcation, with subsequent occlusion. Additional magnetic resonance (MR) imaging and MR angiography could be performed in the six most recent patients : the occlusion and the presence

of the mural thrombus were confirmed. The degree of disability at 3 months was evaluated using the modified Rankin scale (de Haan *et al.*, 1993).

The PET studies were performed according to the steady-state technique with ^{15}O (Frackowiak *et al.*, 1980) between one and two months after stroke onset, when the patients were in a stable condition. The remaining vascular occlusion was confirmed by Doppler sonography of the extracranial arteries prior to the PET examination. Informed consent for PET examinations was obtained from patients or their near relatives. The study was approved by the Hospital Ethical Committee.

A NEURO-ECAT IV PET scanner (EG&G Ortec, Oak Ridge, TN) equipped with 2 rings of detectors, with lateral and axial resolution of 8.1 mm and 14.0 mm respectively, was used. Measurements were performed in high-resolution mode with septa and shadow shields in.

After a phantom scan was performed with an external $^{68}\text{Ge}/^{68}\text{Ga}$ ring source, the head of each patient was positioned to allow accumulation of data from two transaxial planes with their centers 3 mm and 35 mm above the orbito-meatal line. Thereafter, a transmission scan was performed with the external $^{68}\text{Ge}/^{68}\text{Ga}$ ring source for photon attenuation to correct the subsequent emission scans.

For measuring regional cerebral blood flow (rCBF), C^{15}O_2 was inhaled by the patient at a rate of 0.7 GBq/min. After 10 minutes of equilibration, the radioactivity in the head was scanned for 300 seconds. Two samples of arterialized blood were obtained anaerobically at the beginning and at the end of the scan.

For measuring regional metabolic rate of oxygen (rCMRO₂), $^{15}\text{O}_2$ was inhaled at a rate of 1.5 GBq/min, and after an equilibration period of 10 minutes, the scan time was extended to 400 seconds and samples of arterialized blood were taken anaerobically at the beginning and at the end of the scan.

The methods for measurement of radioactivity in the blood samples and of rCBF, regional oxygen extraction fraction (rOEF) and rCMRO₂ have been previously described (Weyne *et al.*, 1987). rOEF and rCMRO₂ values were not corrected by cerebral blood volume values, probably leading to a relative overestimation due to the signal from the non-extracted intravascular ^{15}O (Lammertsma and Jones, 1983).

Three slide reconstructions were obtained 3 mm, 19 mm, and 35 mm above the orbito-meatal line, respectively. In each patient ellipsoid regions of interest (ROI's) with an axial axis of 30mm and a lateral axis of 15 mm (two times the resolution of the camera), covering the whole cortical ribbon of both cerebral hemispheres, and circular ROI's adapted to the size of striatum and thalamus were defined. Corresponding CT planes, performed near the time of the PET examination, were superim-

posed on the PET slices in order to define the infarct core and the peri-infarct zone.

The PET data within the infarct area, the peri-infarct zone, the remaining homolateral hemisphere, and the total contralateral hemisphere were compared to the control values obtained from six persons, exempt of any central neurological disease. The values of rCBF and rCMRO₂ in the contralateral hemispheres were also analysed after adjustment for age as those values decrease with approximately 0.5 % each year with increasing age (Leenders *et al.*, 1990) and our control group was on average significantly older than the patient's group.

Kruskal-Wallis one-way analysis of variance and two-group Mann-Whitney U-tests were utilized for statistical analysis. Statistical significance was set at P values < 0.05.

Results

The demographic, clinical, angiographic and CT data and time of PET examination of the patients with internal carotid artery occlusion, due to cervical dissection, are presented in table 1. The average age of the patients was 46 years (range: 25-64 years) and 60 years (range: 56-66 years) in the control group. Two patients with carotid occlusion by cervical dissection also displayed severe contralateral stenosis without neurological signs to be attributed to this vascular lesion. Five patients had territorial infarcts and the other five cortical borderzone infarcts on CT scans of the brain. The

Table 1

Demographic, clinical, angiographic, and CT data and time of the PET examination of the studied populations (n = 10).

Age, years	
Median	46
Range	25-64
Gender	
Male	8
Female	2
Minor preceding trauma	6
Orgozo score on admission	
Mean (SD)	81 (10)
Range	70-95
Rankin score at 3 months	
Mean (SD)	2 (1)
Range	0-3
Angiographic findings	
Side of occlusion	
Right	9
Left	1
Contralateral stenosis > 75%	2
Location of infarcts	
Cortical middle cerebral artery territory	3
Deep middle cerebral artery territory	2
Cortical arterial borderzone	5
Delay between stroke and PET (days)	
Mean (SD)	42 (8)
Range	30-60

SD : standard deviation

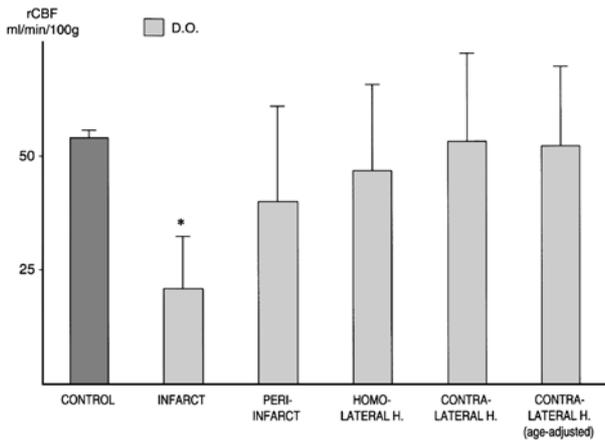


FIG. 1. — Graph comparing the average values with standard deviation of regional cerebral blood flow (rCBF) in the different regions of interest in our patient's population with the control group. rCBF is only significantly decreased in the infarct area (*).

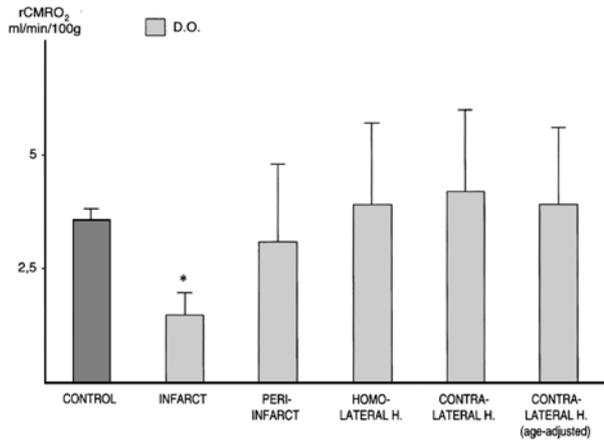


FIG. 2. — Graph comparing the average values with standard deviation of regional cerebral metabolic rate of oxygen (rCMRO₂) in different regions of interest in our patient's population with the control group. rCMRO₂ is only significantly decreased in the infarct area (*).

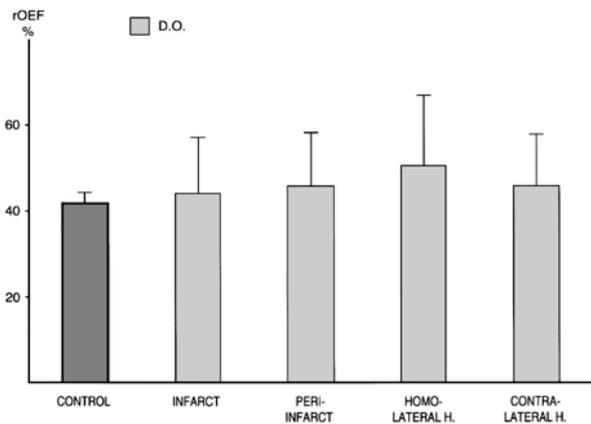


FIG. 3. — Graph comparing the average values with standard deviation of regional oxygen extraction fraction (rOEF) in different regions of interest in our patient's population with the control. rOEF is not significantly different in any region, including the peri-infarct zone in patients.

patients had on average moderate neurological deficits on admission and remained only mildly disabled after three months.

The PET data showed only a significant decrease of rCBF and of rCMRO₂ in the infarct zone but not in the peri-infarct region, the remaining homolateral hemisphere and the total contralateral hemisphere, even after age adjustment (Fig.1-2). rOEF was not significantly different in the various cerebral ROI's of the patient's group as compared to the control group (Fig. 3).

Discussion

Our serial PET study has shown that rCBF and rCMRO₂ are only decreased in the infarct area, without changes in rOEF. The values are compatible with irreversible cerebral damage (Heiss and Herholz, 1994). There is no particular reason why right hemispheric lesions predominated in our series.

Functional imaging studies in carotid artery dissection have rarely be performed in the past. The few single PET studies have shown an area of luxury perfusion in the acute stage and a zone of decreased cerebral blood flow and metabolism, corresponding to the infarct area, after months (Bremerick *et al.*, 1997 ; Rommer *et al.*, 1994).

In our study the peri-infarct zone and the remaining homolateral and the contralateral hemisphere have values for rCBF and rCMRO₂ within the normal range. As the control group was older age the values in the contralateral hemispheres were adjusted for age. There are no studies available on the influence of age on ischaemic damage. Thus, the values in affected hemisphere were maintained as such. As they are significantly different in the peri-infarct regions from those in the infarct core, they can most probably be considered as consistent with normal rCBF and rCMRO₂.

These findings differ from what is observed in symptomatic internal carotid artery occlusion due to atherosclerosis in which the peri-infarct zone displays moderately decreased rCBF and rCMRO₂ (De Reuck *et al.*, 2003) and the contralateral hemisphere decreased rCMRO₂ (De Reuck *et al.*, 1997), suggesting more widespread subclinical ischaemic lesions.

In internal carotid artery occlusion due to cervical dissection the rOEF is not increased in the peri-infarct zone and in the remaining homolateral cerebral hemisphere, indicating the absence of a penumbra or chronic hypoperfusion. The presence of chronic hypoperfusion is considered to be a risk indicator for stroke recurrence in cases of internal carotid artery occlusion by atherosclerosis (Grubb *et al.*, 1998 ; Yamauche *et al.*, 2000). The normal rOEF values in our patients with cervical dissection may be related to the low recurrence risk for stroke in this condition.

In a previous case report we have shown that rCBF and rCMRO₂ increase with time after the internal carotid artery occlusion by cervical dissection although the occlusion remained, suggesting the progressive development of a collateral circulation (De Reuck *et al.*, 2001).

The present PET study argues more for artery-to-artery emboli (Orlandi *et al.*, 1997) or at least for a combination of emboli and temporary hypoperfusion (Caplan and Hennerici, 1998) rather than for a pure haemodynamic event as the cause of the cerebral infarction due to internal carotid artery occlusion by cervical dissection. It also justifies the use of anticoagulants in the acute stage of the stroke in this condition.

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