CHANGES IN CEREBRAL HEMODYNAMICS AFTER CAROTID STENTING: EVALUATION WITH CT PERFUSION STUDIES*

A. TROJANOWSKA (1), A. DROP (1), T. JARGIELLO (2), J. WOJCZAL (3), M. SZCZERBO-TROJANOWSKA (2)

(1) Department of General Radiology Medical University of Lublin, Poland.
(2) Department of Interventional Radiology Medical University of Lublin, Poland.
(3) Department of Neurology Medical University of Lublin, Poland.

SUMMARY
Purpose: To determine changes in cerebral perfusion parameters, based on CT perfusion imaging, in patients after unilateral transluminal angioplasty and stent placement.

Material and methods: 74 patients with symptomatic high – grade internal carotid artery stenosis (>70%) were studied with CT perfusion imaging before and – on average – 70 hours and 172 days after carotid stent placement. There were 50 patients with unilateral carotid artery stenosis and 24 with stenosis and accompanying contralateral internal carotid artery occlusion. CT examination was performed using a multidetector helical CT scanner (Light Speed Ultra Advantage, GE Healthcare, USA). Maps showing the absolute values of cerebral blood flow (CBF), cerebral blood volume (CBV) and mean transit time (MTT) were generated.

Results: In a group with unilateral carotid artery stenosis perfusion deficits were present in 84% of patients, ipsilaterally to stenosis. MTT elongation was noted (6.2-6.8s) together with decreased values of CBF (40-46ml/100g/min) and slightly increased CBV (3.2ml/100g). In this group, 3 days after stenting, 30% of patients had perfusion deficits, and after 6 months only 6%. In a group with carotid artery stenosis and contralateral artery occlusion severe perfusion deficits were noted in both hemispheres and they were present in 100% of patients. 6 months after stenting hypoperfusion was observed only in 17% of patients.

Conclusions: Brain perfusion deficits, observed in a majority of patients with carotid artery stenosis tend to improve considerably after carotid artery stenting, in long – term follow up.

Key words: carotid artery stenosis, cerebral ischaemia, carotid artery stenting, CT perfusion.

RESUMÉ
Objectif : Déterminer les modifications des paramètres de perfusion cérébrale en scanner de perfusion après angioplastie translaminale et pose de stent.

Matériel et méthodes : 74 patients porteurs d’une sténose serrée carotide symptomatique (>70 %) ont été étudiés en scanner de perfusion avant et après (en moyenne 70 heures et 172 jours après traitement) : sténose unilatérale (n = 50), sténose et occlusion de l’artère carotide interne controlatérale (n = 24). L’appareil était un scanner multidétecteurs (Light Speed Ultra Advantage, GE Healthcare, USA). Les cartographies suivantes ont été générées : valeurs absolues du débit sanguin cérébral (CBF), du volume sanguin cérébral (CBV) et temps de transit moyen (MTT).

Résultats : Dans le groupe des patients porteurs d’une sténose unilatérale isolée, les résultats étaient les suivants : déficit de perfusion homolatéral à la sténose chez 84 % des patients, allongement du MTT (6,2-6,8 s), diminution des valeurs du CBF (40-46 ml/100 g/min) et légère augmentation du CBV (3,2 ml/100 g). Dans ce groupe, 3 jours après le stenting, 30 % des patients avaient des déficits de perfusion et après 6 mois seulement 6 %. Dans le roupe des patients porteurs d’une sténose carotide et occlusion de l’artère carotide interne controlatérale, des déficits sévères de la perfusion bihémisphérique étaient retrouvés chez 100 % des patients et une hypoperfusion était observée chez 17 % seulement des patients 6 mois après le stenting.

Conclusion : Les déficits de perfusion cérébrale observée chez la majorité des patients porteurs de sténose carotide tendent à s’améliorer considérablement après stenting carotide lors des contrôles à long terme.

Mots-clés : sténose carotide, ischémie cérébrale, stenting, CT perfusion.

INTRODUCTION
Internal carotid artery (ICA) stenosis is among the most common causes of cerebral ischaemia. It has been suggested, that a higher incidence of ischemic events is associated with abnormal cerebral hemodynamics causing cerebral hypoperfusion. Despite this fact the importance and the influence of hemodynamic factors on the pathogenesis of cerebral ischaemia remains unclear. Therefore, in patients with symptomatic carotid artery stenosis it seems to be advisable to perform brain perfusion studies in order to estimate brain perfusion deficits.

AIM OF THE STUDY
We sought to determine late changes in cerebral perfusion parameters, based on CT perfusion imaging, in patients who have undergone unilateral transluminal angioplasty and stent placement (CAS). We also investigated, whether in patients with internal
carotid artery occlusion stenting of a severely stenotic contralateral carotid artery can establish a long-term improvement in cerebral hemodynamics.

MATERIAL AND METHODS

We evaluated 74 symptomatic patients (fifty two men and twenty two women) aged 52-81 years (mean, 65 years), with unilateral stenosis (> 70% according to the North American Symptomatic Carotid Endarterectomy Trial [NASCET] criteria) of the ICA. All the enrolled patients underwent neurologic and cardiac examinations, electrocardiography, Doppler sonography, and CT angiography of the aortic arch vessels plus CT perfusion examination of the brain at the level of basal ganglia. Fifty seven patients sustained a hemispheric transient ischemic attack and seventeen an ocular transient ischemic attack; all of them were treated with antiplatelet therapy with low-dose aspirin. The degree of stenosis ranged from 70% to 97%. The contralateral ICA was normal or showed a stenosis lower than 30% in fifty patients; in twenty four remaining patients contralateral ICA was occluded. The study protocol was approved by our institutional review board, and informed consent was obtained from patients or guardians in all cases.

CT examination was performed using a multidetector helical CT scanner (Light Speed Ultra Advantage 8-row, GE Healthcare, USA) with the following protocol:

- non-contrast enhanced transaxial CT of the whole brain (section thickness 2.5mm, no overlap, slices parallel to orbito-meatal line, 80kVp, 120mAs);
- dynamic CT perfusion imaging (45seconds of constant scanning at the level of basal ganglia, 4x5mm slices, no overlap, 120kVp, 250mAs). Contrast medium administration – 50ml, delay 5 sec, bolus 4.5ml/s.
- CT angiography from aortic arch to vertex (section thickness 1.25mm with 0.6mm overlap, 120kVp, 180mAs, 80ml of iodine non-ionic contrast medium in bolus, at the rate of 4ml/s, delay – Smart Prep) (figure 1).

Perfusion scans were performed at the level of the basal ganglia (section thickness 4x5mm, field of view – head, matrix 512x512, 50ml of iodine non-ionic contrast medium at the rate of 4ml/s). A preliminary

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**FIG. 1.** – CT examination in evaluation of carotid artery stenosis. Volume rendering (a), Advanced Vessel Analysis (b) and virtual endoscopy reconstructions (c).

**FIG. 2.** – CT examination in evaluation of carotid artery stent placement. Volume rendering (a), MPR (b) and virtual endoscopy reconstructions (c).

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study was carried out to exclude the presence of MCA or border zone infarcts. Maps showing the absolute values of cerebral blood flow (CBF), cerebral blood volume (CBV) and mean transit time (MTT) were generated by deconvolution of the tissue enhancement curves from 2x2 pixel blocks of the brain with an intracranial artery contrast enhancement curve. Localized CBV, CBF and MTT values were calculated for different vascular territories (middle, anterior, and posterior cerebral arteries) in each hemisphere.

To evaluate MTT, CBF and CBV maps, regions of interest (ROIs) were positioned, bilaterally, in the vascular territory of the distribution of the MCA and border zone by using the cortical and intracerebral boundaries proposed by van der Zwan et al [9] and modified by Hupperts et al [2]. For each variable one-way analysis-of-variance tests were performed to assess differences between the stenotic and contralateral sides. Excel 98 was used for data analysis.

All patients with internal carotid artery stenosis afterwards underwent stent placement and were studied with CT angiography and perfusion imaging on average 70 hours and 172 days after stenting procedure (figure 2).

In all cases carotid SILVER stent (Cook) was used together with neuroprotection device (Angioguard).

RESULTS

In a group with unilateral carotid artery stenosis perfusion deficits were present in 84% of patients, ipsilaterally to stenosis. A marked MTT elongation was noted (6.2-6.8s) together with decreased values of CBF (40-46ml/100g/min) and slightly increased CBV (3.2ml/100g), comparing to contralateral hemisphere (figure 3). CBV values give information about the current status of blood vessel capacity; the increased value of this parameter indicates that brain blood vessels are dilated, most probably due to partially insufficient brain circulation autoregulation mechanisms.

Mean values of perfusion parameters for the stenotic side (SD in brackets):  
- CBF 40-46ml/100g/min (±9.1);  
- CBV 2.9-3.2ml/100g (±0.4);  
- MTT 6.2-6.8s (±0.6).

Mean values of perfusion parameters for the contralateral hemisphere (normal side):  
- CBF 55-59ml/100g/min (±12.6);  
- CBV 2.7-2.9ml/100g (±0.5);  
- MTT 3.1-3.4s (±0.7).

All patients underwent follow-up perfusion examination 3 days after CAS. In this group, 15 patients (30%) still had statistically significant perfusion deficits. Mean values of perfusion parameters in stenotic side for this group were as follows (figure 4):  
- CBF 47-51ml/100g/min (±9.8);  
- CBV 2.8-3.2ml/100g (±0.4);  
- MTT 4.1-4.3s (±0.9).

CBF, CBV and MTT mean values of perfusion in the contralateral hemisphere remained unaffected.

On the next follow-up examination, which took place on average 170 days after CAS, all patients were examined. Brain perfusion deficits were still noted in 4 patients (8%). Mean values of perfusion parameters in stenotic side for this group were as follows:  
- CBF 42-49ml/100g/min (±9);  
- CBV 2.7-3.0ml/100g (±0.5);  
- MTT 4.1-4.5s (±1.2).

CBF, CBV and MTT mean values of perfusion in the contralateral hemisphere remained unchanged.

In a group with one stenotic carotid artery and contralateral occluded carotid artery, severe perfusion
deficits were noted in both hemispheres and they were present in 100% of patients (figure 5).

Mean values of perfusion parameters in stenotic side hemisphere for this group were as follows:

- CBF 36-41 ml/100g/min (±10.6);
- CBV 3.4-3.6 ml/100g (±0.5);
- MTT 6.1-6.8s (±0.7).

Mean values of perfusion parameters in contralateral hemisphere (the side with carotid artery occlusion):

- CBF 29-32 ml/100g/min (±8.1);
- CBV 3.6-3.9 ml/100g (±0.4);
- MTT 8.1-9.8s (±1.3).

3 days after CAS perfusion deficits were present in six (25%) patients ipsilaterally to stenosis and in twelve (50%) patients contralaterally, among all 24 patients examined.

Mean values of perfusion parameters in stenotic side for this group:

- CBF 48-52 ml/100g/min (±8.6);
- CBV 3.0-3.2 ml/100g (±0.4);
- MTT 4.2-4.8s (±1.4).

Mean values of perfusion parameters in contralateral hemisphere (with carotid artery occluded):

- CBF 40-46 ml/100g/min (±9.6);
- CBV 3.4-3.7 ml/100g (±0.5);
- MTT 6.1-6.8s (±1.9).

6 months later in follow-up examination of all 24 patients, hypoperfusion was observed in four patients (17%) ipsilaterally and in six patients (25%) contralaterally (figure 6).

Mean values of perfusion parameters in stenotic side for this group:

- CBF 48-56 ml/100g/min (±9.6);
- CBV 3.0-3.4 ml/100g (±0.5);
- MTT 4.1-5.1s (±1.6).

Mean values of perfusion parameters in contralateral hemisphere (with carotid artery occluded):

- CBF 39-46 ml/100g/min (±9.6);
- CBV 3.4-3.6 ml/100g (±0.5);
- MTT 6.2-7.0s (±1.9).

**DISCUSSION**

Hemodynamically significant stenoses (meaning, capable of causing local hemodynamic changes at the point of stenosis and considered over 70% based on NASCET criteria) are frequently encountered in clinical practice. It is known and proven now, that the risk of developing an ischemic event is higher in patients with reduced cerebrovascular reactivity than in those in whom cerebrovascular reactivity is preserved [1, 6, 8, 10]. For this reason, different tools have been tested in order to evaluate cerebral hemodynamics. One of them is transcranial Doppler sonography, which represents a noninvasive and reliable technique that has been used in the last few years to measure, in the intracranial arteries, the flow variations in response to dilatatory stimuli, such as acetazolamide or CO₂ inhalation [7]. Other imaging techniques to study cerebral hemodynamics are PET, SPECT, perfusion-weighted MR imaging and recently CT perfusion imaging. Perfusion imaging based on computed tomography allows the evaluation of some fundamental parameters to study cerebral hemodynamics, such as cerebral blood flow, cerebral blood volume and mean transit time. CT perfusion imaging can be easily performed as completion of a standard brain CT examination, with a small increase in the time and costs of the imaging technique.

In our study, we evaluated the cerebral hemodynamics alterations in two groups of patients: one with symptomatic unilateral carotid stenosis and the other with accompanying contralateral artery occlusion, by using CT perfusion studies. Our data show that perfusion deficits are present in 42 patients (84%) with 70-97% unilateral carotid stenosis. Statistically significant increase of CBV and MTT together with the decrease of CBF was observed in the hemisphere supplied by the stenosed ICA. Mean transit time elongation is substantial, proportionally to the degree of stenosis and blood flow decrease. Cerebral blood volume is only slightly increased.
This parameter provides information concerning brain blood vessels status (dilatation or stricture). Increased values of CBV inform that blood vessels are dilated, therefore their autoregulation mechanisms are impaired. This is a potentially dangerous situation, because after successful stenting procedure, when normal blood flow is restored in carotid artery, such dilated vessels receive increasing volume of blood (luxury perfusion). In this moment, in a healthy subject, brain autoregulation mechanisms should act immediately, causing stricture of such blood vessels. When this function is impaired (eg. due to a long standing hypoperfusion) dilated vessels will not constrict properly and there is a potential risk of having a haemorrhagic stroke in such patients. Thus, increased CBV values in perfusion examination are negative predictive factors and patients with increased CBV are defined as patients at higher risk, comparing to group with normal CBV values.
Our data agree with those recently reported by Maeda et al. [5]. These authors describe differences in MTT between the normal and the symptomatic hemisphere in distal vascular territories of cerebral arteries in patients with ICA stenosis. This finding is confirmed in our study.

Hemodynamic asymmetries between the hemispheres in patients with symptomatic carotid artery stenosis and contralateral occlusion were also reported by Kim et al. [3], who also correlated the prolongation of MTT with the vascular reserve capacity data obtained with SPECT before and after intravenous administration of acetazolamide. Based on our results and the above mentioned data from other studies, we suggest that hemodynamic changes occur in both cerebral hemispheres in cases with symptomatic arterial stenosis and contralateral occlusion of the ICA. The presence of contralateral occlusion will most probably lead to severe hemodynamic impairment. This can be explained by the lack of efficient cross-circulation at the level of circle of Willis in cases, where contralateral flow is severely impaired or non-existent. In such cases blood from the hemisphere on the stenotic side crosses to the contralateral hemisphere in order to partially restore brain perfusion, which in this hemisphere is altered much more than in hemisphere on the stenotic side. Finally, we encounter the status with cerebral perfusion defects, present in both hemispheres. A marked cerebral hyperperfusion in one hemisphere is explained by the severe stenosis of the carotid artery. Perfusion deficits visible in contralateral hemisphere are the obvious result of contralateral carotid artery occlusion. Even with properly functioning circle of Willis and excellent cross-circulation the impaired blood flow from the single (and stenotic) carotid artery is insufficient to maintain proper brain perfusion. The most affected is the hemisphere on the side of carotid artery occlusion. Based on this mechanism it is easy to explain, why after carotid artery stenting a considerable improvement of brain perfusion concerning two hemispheres is noticed.

CONCLUSIONS

Based on our study, it can be stated, that in cases of significant carotid artery stenosis there is inadequate compensation of impaired blood flow to ipsilateral hemisphere, what results in brain perfusion deficits. Hypoperfusion observed in CT perfusion studies tends to improve considerably after carotid artery stenting, in short- and long- term follow up. Also contralateral carotid artery stenting in patients with symptomatic internal carotid artery occlusion induces cerebral haemodynamics improvement not only on the side of stent placement but also on the side of carotid artery occlusion in majority of cases.

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REFERENCES