HEMODYNAMIC CHANGES OF SEVERE CAROTID ATHEROMATOSIS PRE AND POST ENDARTERECTOMY IN THE CASE OF A CORONARY PATIENT WITH ISCHEMIC STROKE

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ABSTRACT

Nearly 25%-30% of ischemic strokes are due to atherosclerosis of the carotid bifurcation. Cerebrovascular reactivity (CVR) is an indicator for testing hemodynamic status of cerebral circulation. The purpose of the presentation was to determine the effects of CEA (endarterectomy) on cerebral hemodynamics with cerebral hemodynamic change tracking, by measuring the average flow velocities (MFV) in the ipsilateral and contralateral middle cerebral artery (MCA) severe carotid stenosis and pulsatility index (PI) by the help of the Transcranian Doppler (TCD) and the study of CVR (cerebrovascular reactivity) by performing BHT (Breath-holding test) both before and at 7 days and at 2 and 4 months post intervention, as well as cerebral hemodynamic parameters determining through Cerebral Perfusion CT and correlation with risk factors and prior stroke event. Using ultrasound methods ECD (Extracranial Doppler) and TCD (Transcranial Doppler) and imaging (Perfusion Cerebral CT, angioCT cervical region, angiocoronarography) allowed: increased detection of patients at risk of stroke and myocardial infarction, stroke diagnosis of ischemic sites, the calculation of hemodynamic parameters of cerebral circulation at patients with coronary stenosis and carotid stenosis, occlusion with stroke up, TIAs or stroke risk and heart attack.

Key words: carotid stenosis > 70%; transcranian Doppler – breath-holding test, cerebrovascular reactivity, CT perfusion, carotid endarterectomy

INTRODUCTION

Stroke represents a pathology with important socio-economic implications, with serious consequences for patients and which poses medical and social problems both in terms of urgent therapeutic attitude and in terms of recovery in sub acute and chronic stages of the tissue and brain functions. Nearly 25%-30% of stroke occur due to arterial embolisation or occlusion related to the carotid bifurcation. (1) So, the ultrasound examination and the imaging play a crucial role both in the diagnosis of stroke in the hyper acute/acute stage, as well as in detecting and establishing a prophylactic treatment of the patients who present a stroke risk, in the setting of a clinical management and in the monitoring of a prevention treatment. (2) TCD and functional imaging play a key role in presenting cerebral hypo perfusion in patients with potential increased risk of stroke. (3) The progressive narrowing of the arteries by thickening with atheroma and the embolism started from the level of irregularities on the surface of the ulcerated plaque cause the decrease of cerebral perfusion until the myocardial ischemia and the infarction appear. (4) European and American trials controlled randomized have shown that carotid endarterectomy is the surgery to

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be performed in patients with symptomatic carotid stenosis over 70 %. (5)

Cerebral perfusion can be studied using different radiological techniques such as convectional angiography DSA (capillary phase), PET and SPECT. PET and SPECT are inaccessible in current clinical practice, where MRI and CT perfusion can be merely applied to common devices. Perfusion maps of rCBV (cerebral blood volume) and rCBF (cerebral blood flow) show hypointense signal in areas with reduced perfusion and the TP (time to peak) maps show hyperintense signal. (6) The CT allows in vivo quantification of cerebral perfusion (blood supply to the brain parenchyma through the capillary network). 5 types of functional maps are obtained, each characterizing the spatial distribution in the cerebral parenchyma of a hemodynamic parameter: cerebral blood volume (CBV), cerebral blood flow (CBF), bolus arrival time in the area of interest (TS), mean transit time (MTT), time to reach the maximum value also called the peak time (TP). (6)

Cerebrovascular reactivity is an indicator for testing hemodynamic status of cerebral circulation, which is a regulating mechanism, represented by the ability of cerebral arterioles to dilate additionally or create vasoconstriction to maintain a constant cerebral blood flow in different conditions of local or systemic demand. It was proven that changes RCV represent an important risk factor for stroke and TIA at patients with stenosis and carotid occlusion (7).

There are several techniques for evaluation of RCV, including PET (positron emission tomography), SPECT (single photon emission computed tomography), Xe-CT (enhaced stable xenon-computed tomography), and DSC-MRI (dynamic susceptibility contrast magnetic resonance imaging) these methods are expensive, time consuming, need special equipment, radiation, so they are not used for routine clinical examination (8). Transcranial Doppler monitoring is today a well-documented method and with reliable results being a relatively simple, non-invasive, repeatable and less costly to evaluate RCV. There are three methods to assess the CVR with TCD, all these methods use as vasoactive stimulus, increasing the partial pressure of CO2 by enriching the breathing air with CO2, administration of intravenous acetazolamide or prolonged apnea, the results obtained by all these methods bearing comparison with the assessment of cerebral hemodynamics (9). The RCV assessment through the apnea teast is made by using BHI (breath-holding index) which is a usual method of screening. (10).

CASE PRESENTATION

We assessed a patient with symptomatic severe carotid stenosis and contralateral carotid occlusion with chronic ischemic stroke sites, where we tried to emphasize cerebral hemodynamic changes by measuring the average flow velocities at MCA and pulsatility index before and after making unilateral carotid endarterectomy and double coronary artery bypass and monitoring the patient later with transcranial Doppler evaluation every 2 months for 4 months using TCD to determine BHT and RCV calculation both before and at 7 days and at 2 and at 4 months post interventional as well as calculation of preinterventional hemodynamic parameters through cerebral perfusion CT and correlation with risk factors and stroke and coronary event.

Male, 78 years old, with multiple cardiovascular risk factors (hypertension for about 15 years, former smoker (about 58 years -30 cigarettes/day), type II diabetes mellitus for 10 years, dyslipidemia, with chronic obliterative arterial disease for 23 years, with trombendarterectomy at left common femoral artery 9 years ago for which he had therapy with an oral anticoagulant treatment, Sintrom, for two years. For the past eight years suffered from three transient episodes of left upper limb distal paresthesias and left facial paresis type central, and a subtle left hemiparesis for approximately 2 weeks which is why the patient visits the neurologist, refuses hospitalization, performes a brain MRI, cerebral AngioMRI ambulatory that shows multiple lacunar infarcts bilateral supratentorial more numerous on the right side and a right parietal ischemic lesion in late subacute stage, and the Angio sequence one can distinguish a right carotid stenosis without indicating the degree of atheromatosis. The patient does not continue conducting further investigations to establish the degree of carotid stenosis and eventual surgery, stops smoking and has antiplatelet therapy with Clopidogrel 75 mg / day that is interrupted after 5 years and Atorvastatinum 40 mg / day 2 months, 20 mg / day 2 months, then 10 mg/day that is interrupted after 4 years. In this period and until 2013 he did not present any clinical neurological event.

In March 2013 the patient visits the neurologist and cardiologist for chest pain with angina, debuted at rest, jaw irradiation, a transient episode of right upper limb distal paresthesias lasting 2-3 minutes, 7 days ago, a transient episode of right facial asymmetry with a duration of about 5 minutes, 5 days ago and balance disorders with onset in standing and walking for about 3 months and accentuated in the last month.

On **neurological examination** there is evidence of unbalanced gait with slight wide support, slight interference to the right with unilateral walking stick, Romberg + unorganized oscillations, sequela right hemiparesis, evidence of ROT slightly right> left, cranial nerves normal relations. The following tests are performed: **EKG:** sinus rhythm, FC -81 beats/minute, intermediate QRS axis without pathological ischemic changes, **laboratory analysis**: Hb – 14.4 to 12, 8 g%, Ht – 38.7%, Leucocites – 7340/ mm3, Glucose – 99 mg / dl, Creatinine – 1,88-1,5-1,3 mg%, Cholesterol – 156 mg%, AST – 29U/L, ALT – 21U/l, Na – 144-142 mEq/l, K – 4.2 to 3,8mEq/l. **Cardiac Ecocardiography:** VS normal size, EF = 50%, mitral regurgitation stage II, cusp fibrosis, calcification of the posterior mitral annulus, tricuspid regurgitation stage I. **Doppler Carotid Ultrasound** is carried out that shows: right ICA occlusion, severe stenosis stage V in about 85-90% left ICA at origin. Heterogeneous atheroma plaque, predominantly hyperechoic, predominantly calcified, on distal wall left at ICA origin to the of size of 1.3 cm length / 4.2 mm height determining a stenosis of approximately 85-90%. Left vertebral artery portion V0, V1 shows stenosis of approximately 50%.

It was decided to continue the investigation in order to confirm the severe carotid stenosis through a CT Angiography of the cervical region and the preparation for an endarterectomy surgery. **The CT Angiography of the cervical region** showed that the aortic arch had a diffuse atheromatous with calcified plaque, without stenosis and without aneurismal dilatation. The right internal carotid artery shows a chronic occlusion after scanning. The left internal carotid artery shows a stenotic lesion with an emergence of more than 90 % through mixed atheromatous plaques predominantly non-calcified. The left vertebral artery shows a stenotic lesion of 50% of the proximal segment. The other arteries of the carotid axis and and the subclavian and vertebral arteries show no significant atheromatous lesions. A **Coronary angiography** is done which shows a balanced coronary system, an ACD diffuse atheromatous vessel, it also shows multiple stenotic atheromatous plaques.TACS shows in the proximal segment a stenotic lesion of 50% with an ulcerated plaque appearance, ACx shows a distal stenotic lession of 50-75%, ADA shows in the proximal segment a stenotic lesion 75- 90%.

Cerebral CT perfusion: In the frontal right lobe can be observed the presence of cortico-subcortical hypodense lesion measuring 3.5 / 2.5 cm without a penumbra area without residual vascularization; there are also hypodense areas, indicating hypoperfusion in the right semi-oval center. The hemodynamic parameters of the cerebral CT perfusion: the MIP image emphasizing the hypoperfusion area on the right of the MCA territory comparing to area 1a from the left MCA territory. Cerebral blood volume (CBV) – average value: 32.01 + / 20.1ml/100g in region 1a and 28.7 + / -17.9ml/100g hypoperfusion in region 2a; The ratio of the two examined areas is R- 0.90 in the hypoperfusion

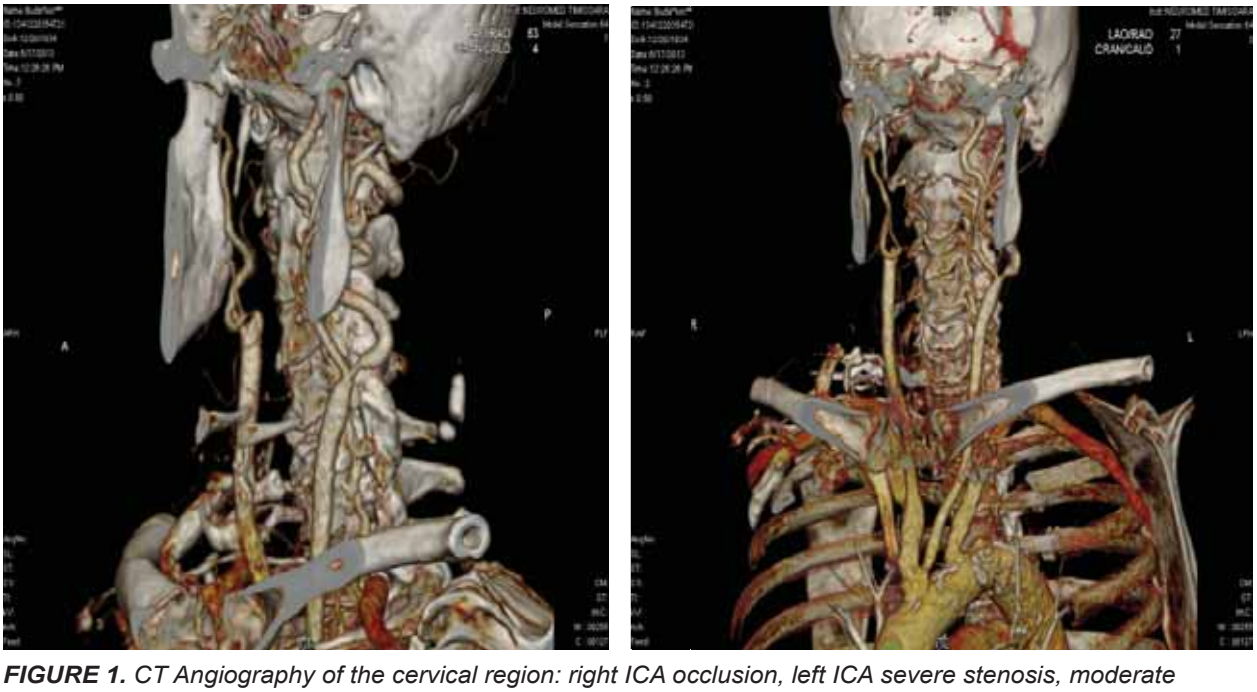

FIGURE 1. *CT Angiography of the cervical region: right ICA occlusion, left ICA severe stenosis, moderate stenosis of the left vertebral artery*

area comparing to 1.11 in the contralateral hemisphere; cerebral blood flow (CBF) – average value: 52,9+/-37.5 ml/100 g/min in area 1a and 48,0+/-35.4 ml/100g/min hypoperfusion in area 2a; The ratio of the two examined areas is R- 0.90 in the hypoperfusion area comparing to 1.10 in the contralateral hemisphere; The time to reach the maximum value is also called time peak (TP) – average value: 11,65+/-1.74s in area 1a and 12,65+/-2.06s hypoperfusion in area 2a; The ratio of the two examined areas is R- 0.92 in the hypoperfusion area comparing to 1.08 in the contralateral hemisphere; MTT-CBV/CBF – 36.29 s in area 1a and 35.87 s hypoperfusion in area 2a.

Following the ultrasound investigation (Extracranial Doppler) and imaging investigations (CT Angiography of the cervical region, Coronary angiography) it was decided to perform a left carotid endarterectomy and a double coronary artery bypass. In order to monitor the hemodynamic parametres and to highlight the degree of impairment of the cerebral perfusion a Transcranial Doppler is performed to be able to calculate the CVR through BHT.

Patient was monitored pre surgery, to detect lesions and the day prior to surgery (maximum period is 2 weeks) and 7 days post surgery, two and four months post surgery with cerebral hemody-

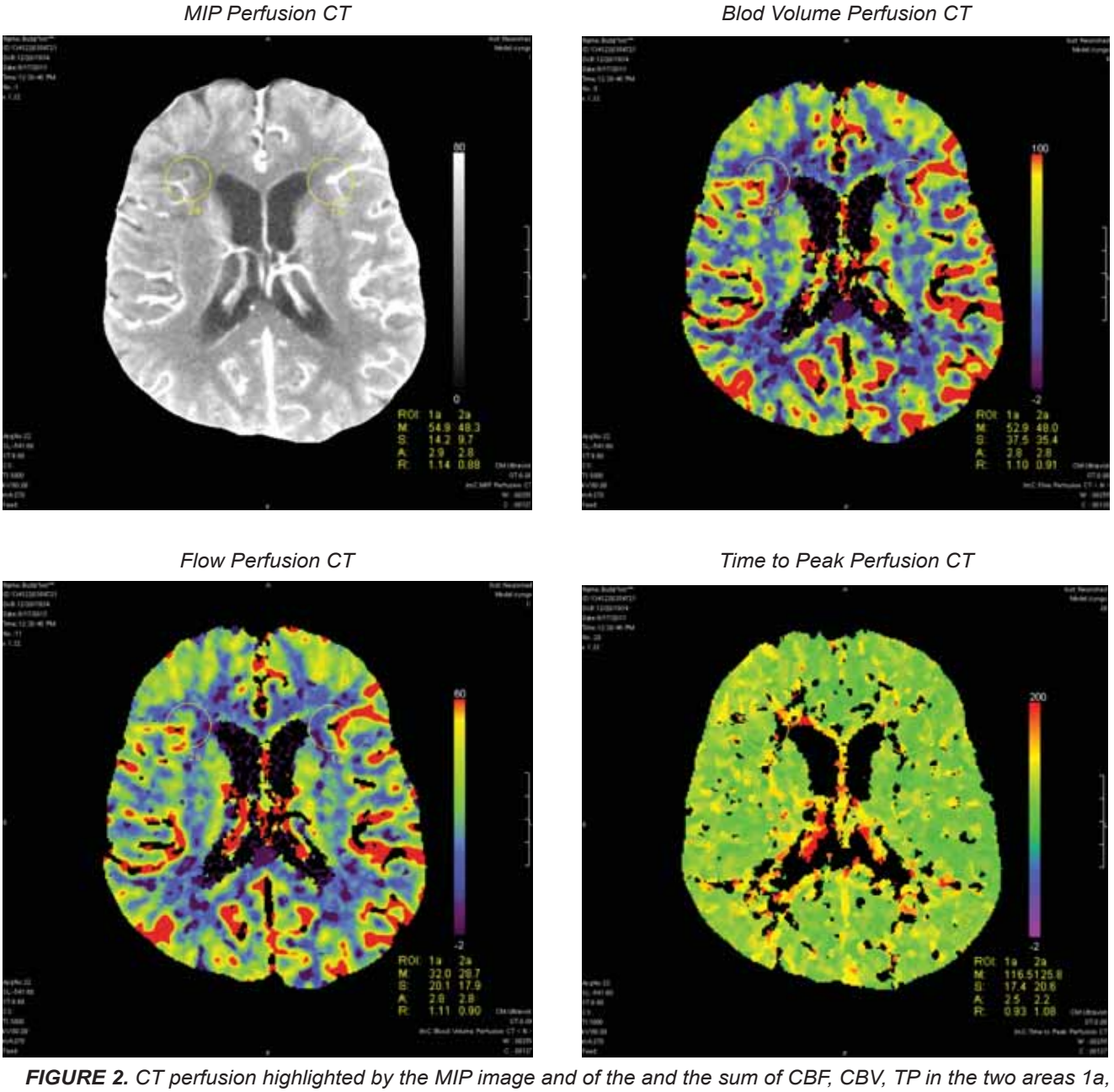

FIGURE 2. *CT perfusion highlighted by the MIP image and of the and the sum of CBF, CBV, TP in the two areas 1a, 2a examined by highlighting the hypoperfusion in area 2*

namics monitoring by TCD with CVR determination by measuring BHT. Evaluations were performed by a Transcranial Doppler of 2 MHz (ESAOTELAB) with Doppler recording images in real time. A temporal window with sound system MCA at a depth of 40-50 mm was used and recording of mean flow velocity and pulsatility index calculation, which is the peak to peak (max and min) velocity divided by mean velocity at the MCA during a cardiac cycle; the normal values for the mean flow velocities at MCA at healthy individuals is between 81 + / -13 and IP is between 0.7 to 1.1, these values are influenced by several factors. (4)

During normal breathing of the air in the room, mean flow velocities were recorded at the level of MCA and IP, after a breath of 1 minute, and then patients were instructed to hold their breath for 30 seconds after a normal inspiration, this time being considered enough to get the increases in the mean velocities on the MCA. During the procedure, the MFV on MCA and IP were recorded continuously, being rated only average values at the end of apnea period this representing the arithmetic average of the higest mean flow velocities during two respiratory cycles (about 10 seconds of apnea).(8) BHI was calculated as a percentage divided by apnea time (30 seconds) multiplied by the difference between average brain speed after apnea and before divided by previous speed): BHI = 100 * 1/Tapnee (MFVapnee-MFVbazal) / MFVbazal (% / s). Normal values for BHI for MCA published by Sylvestrine was 1.2 + / -0.6% / s, values below 0.5 are considered pathological.(10)

TABLE 1. *TCD hemodynamic values ipsi and contralateral severe stenosis pre intervention monitored through TCD*

Doppler values	preCEA	
MCA	**Ipsilateral**	**Contralateral**
MFV-normal (cm/s)	24.3	28.2
IP	0.5	0.6
MFV-BHT(cm/s)	28,1	32.1
CVR(%/s)	0.51	0.45

MFV-BHT was measured at the level of MCA ipsilateral carotid stenosis increased from 24.3 cm /s to 28.1 cm/s but the CVR had a value of 0.51%/s being pathological, representing hypoperfusion in the area of symptomatic stenosis. Contralateral MFV increased from 28.2 cm/s to 32.1 cm/ s after apnea with CVR 0.45% / s, this signifying hypoperfusion of contralteral stenosis, being more obvous in the carotid occlusion.

During **carotid surgery** (11) are shown, in the left common carotid, an atheromatous plaque which comprises the entire circumference of the vessel, soft tissue, calcified, with an irregular surface, spreading from the bifurcation of the carotid to the beginning of left internal carotid artery, the lesion is anfractuous, calcified at the beginning of the internal carotid artery thus causing critical stenosis which also included the ostial of the external carotid artery. A left endarterectomy is performed to remove the atheromatous lesion and, saphenous vein patch plasty with internal autologous – plasty of widening of the bifurcation of the common carotid and of the origin of the left internal carotid artery.

A myocardial revascularization is performed through double coronary artery bypass grafting in extracorporeal circulation with: left internal mammary artery to left anterior descending artery, internal autologous saphenous vein graft on obtuse marginal I.

During the surgery, there were no neurological incidents. Postoperative the patient did not present headaches, confusion, or increases in the blood pressure and there were no neurologic or coronary events.

TABLE 2. *TCD: pre CEA and coronary artery bypass and Post1CEA after 7 days and Post2CEA in 2 months, with significantly improved values of MFV, IP, CVR and of the restoring cerebral perfusion*

Doppler values	PreCEA		Post1CEA		Post2CEA	
MCA	**ipsi**	**contra**	**ipsi**	**contra**	**ipsi**	**contra**
MFV-normal	24.3	28.2	33.8	31.2	35.1	32.4
IP	0.5	0.6	0.8	0.8	0.9	0.8
MFV-BHT	28.1	32.1	42.3	38.3	44.1	40.2
CVR(%/s)	0.51	0.45	0.82	0.75	0.84	0.79

Post ipsilateral endarterectomy in both cases 7 days and 2 months after showed an increase of the basal values MCA MFV from 24.3 cm / s to 33.8 cm / s (7 days after) respectively a 35.1 cm / s (2 months after) as well as of the IP from 0.5 preCEA to 0.8 (7 days after) respectively 0.9 (2 months after). Contralateral severe stenosis after 7 days post-CEA showed a slight increase of MFV-MCA from 28.2 cm / s to 31.2 cm preCEA / s 7 days after and and approximately equal values 2 months after respectively 32.4 cm / s but showing slightly lower values than ipsilateral stenosis and better values 7 days after. The IP increased contralateral from 0.6 to 0.8 both at 7 days and 2 months post- CEA.MFV-BHT increased both ipsi and contralateral stenosis both at 7 days and 2 months post- CEA with better values for ipsilateral stenosis. CVR (% / s) has significantly improved both ipsi and contralateral ste-

nosis, ipsilateral stenosis 7 days after the values increased from 0.51 to 0.82 and contralateral stenosis from 0.45 to 0.75 and 2 months after the values have increased ipsilateral to 0.84 respectively contralateral 0.79, with better values for ipsilateral stenosis, this being due to hypoperfusion of the contralateral hemisphere due to the occlusion of the right ICA.

Figure 3, 4 represent Carotid Doppler – Ultrasound tomography 2 months post endarterectomy.

The patient was evaluated in 4 months time showing favorable cerebrovascular parameters, the patient did not present any cerebrovascular or coronary events

At 4 months post-endarterectomy, the MFV bazal decreased slightly comparing to the 2 months after values both ipsilateral and contralateral stenosis, and from 35.1 cm / s to 32.4 cm / s ipsilateral and contralateral to 32.4 cm / s to 31.8 cm / s while the IP has maintained approximately constant values during the two months postCEA. At 4 months postCEA, MFV-BHT increased slightly ipsilateral stenosis and decreased slightly contralateral stenosis, while CVR values (% / s) increased slightly

TABLE 3. *TCD: Post CEA and coronary artery bypass 2 months and 4 months, having equal values of MFV, IP, with a slight increase in CVR, and maintaining normal cerebral perfusion with a slightly better ispilateral stenosis*

Doppler values	Post2CEA		Post3CEA	
MCA	**ipsilatera**	**contralateral**	**ipsilateral**	**contralateral**
MFV-bazal	35.1	32.4	34.9	31.8
IP	0.9	0.8	0.8	0.8
MFV-BHT	44.1	40.2	44.6	39.9
CVR (%/s)	0.84	0.79	0.91	0.84

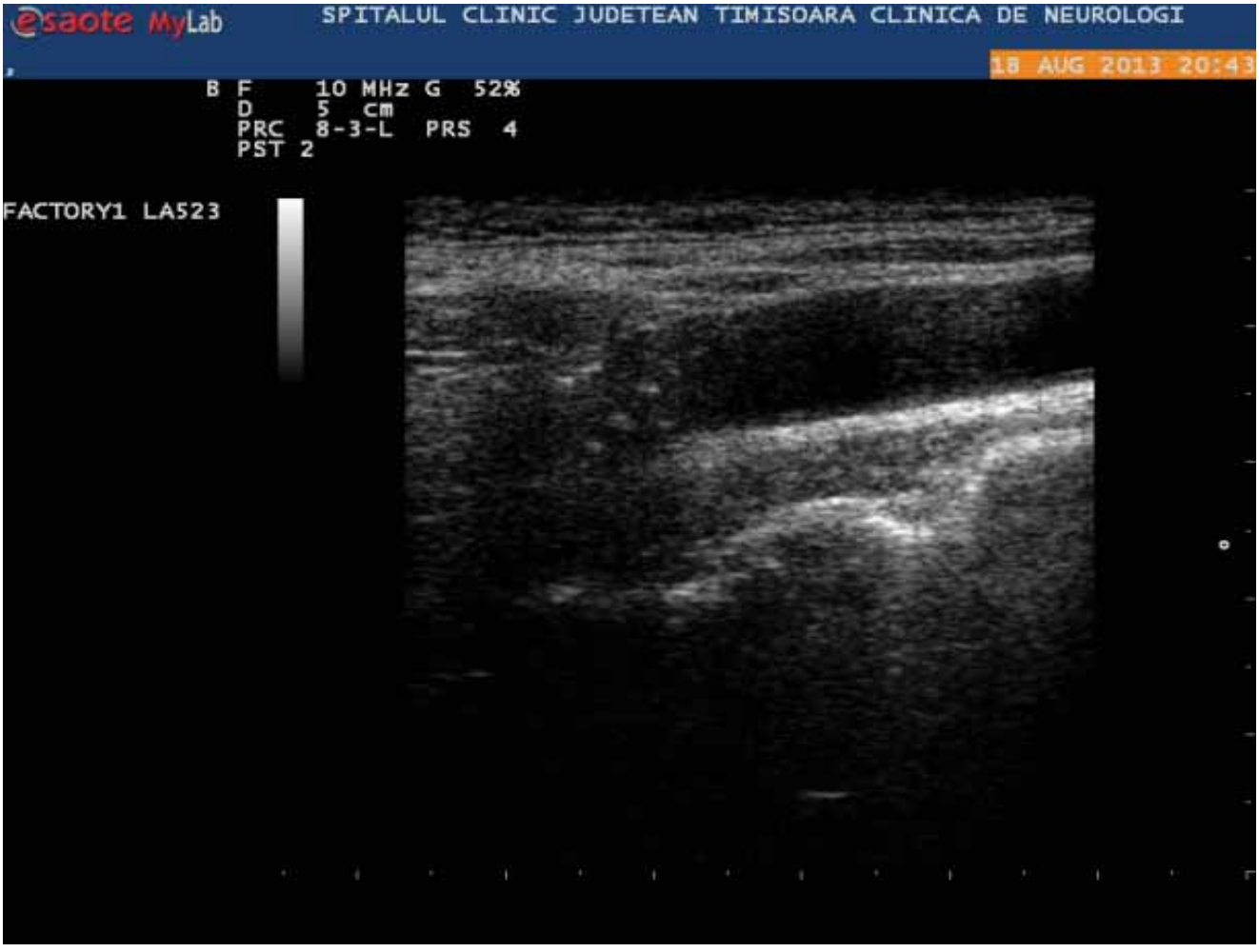

FIGURE 3. *Right ICA occlusion*

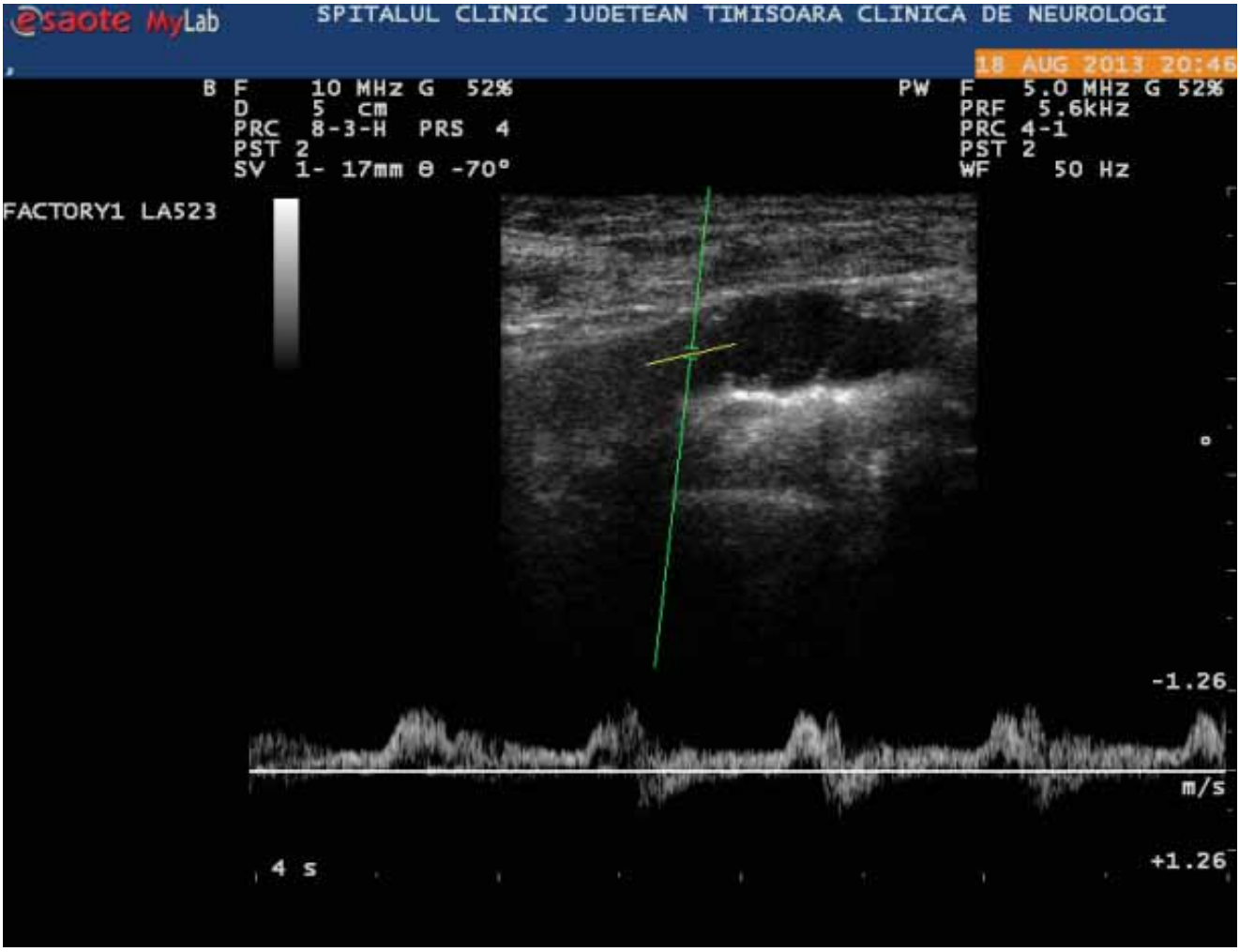

FIGURE 4. *Post endarterectomy status left ICA*

compared to the two months postCEA values, both ipsilateral from 0.84 to 0.91 and contralateral stenosis from 0.79 to 0,84 maintaining better values ipsilateral stenosis respectively 0.91 compared to 0.84.

The patient followed a controlled sodium diet, hypolipidic diet, hypoglucidic, monitored BP values, glucose, cholesterol, continued treatment with platelet antiaggregant, statin, hypotensive medication presenting a favorable evolution.

DISCUSSION

The hemodynamic parameters measured by CT Perfusion have shown that there is an hypoperfusion area corresponding to the carotid occlusion, with slightly higher values of CBF, CBV, MTT being in the severe carotid stenosis territory, and being necessary to perform left carotid endarterectomy to improve the cerebral perfusion in the 2 hemispheres.

The endarterectomy changes the cerebral hemodynamics with improved cerebral perfusion through CVR with the help of TCD. In 7 days after the surgery it was shown an improvement of MFV, IP, CVR through adjusting the cerebral perfusion, both ipsilateral and contralateral with better values for ipsilateral, and through the ability of the cerebral arterioles to produce vasoconstriction to maintain a constant cerebral blood flow.

TCD showed an increase of MFV in 2 and 4 months after surgery both ipsilateral and contralateral, this aspect can be interpreted by increasing the perfusion pressure as a consequence of the return to a normal diameter and flow in the ICA postCEA. Similar results were reported post CAS (12) or CEA. (13,14). An increase of the MFV ipsilateral stenosis was observed in 2 and 4 months compared to 7 days post intervention and it was observed a slight increase contralateral stenosis but with lower values than ipsilateral, higher in 2 months than in 7 days and in 4 months post-CEA. Similar results were observed in another study that monitored patients post-CEA and showed that the lack of increase of MFV contralateral after surgery was due to the presence of severe stenosis and of contralat-

eral chronic hypoperfusion (15). This also happened in the case of this patient who presented contralateral carotid occlusion. In other studies (16), there were not observed significant contralateral increases, while others studies showed a moderate contralateral increase as a consequence of collateral flow through the anterior communicating artery post-CEA (17).

IP increased bilaterally 7 days after the surgery, this represents the vasoconstriction ability of the arteriolar resistance in order to maintain a significant increase in flow within the ICA territory post-CEA. Similar results have been reported post- CAS (12). A study that monitored patients with CAS showed an increase of IP and a slight decrease of MFV as a result of vasoconstriction of the mechanism of self-regulation reflected by an increase of IP (14), and another study that monitored patients with CEA, revealed that the IP is a better predictor for the risk of hyperemia and stroke during and after surgery (15,18).

2 months post-intervention the increase of MFV values compared to pre-intervention values were maintained compared to those of 72 hours after, with slightly better values of ipsilateral stenosis, this indicating an improvement in the cerebral perfusion. The 4 months after values have increased compared to the pre-CEA values but they decreased slightly compared to the two months values, this signifying a return of cerebral perfusion in chronic stage. IP increased after 2 months compared to the beginning and remained constant from 4 months compared to 2 months in both hemispheres, with slightly better values ipsilateral. Similar results were reported after CAS where an increase of MFV and IP was observed with statistically significant values of ipsilateral stenosis, this is due to the vasoconstriction at the arteriolar resistance on hyperemia in response to unilateral perfusion rehabilitation and the restoration of self-regulation mechanism(16). Similar results were observed post-CAS (19). Another study that monitored patients postCEA reported similar results, with an improvement and a normalization of the brain parameters in patients that were monitored from 3 to 12 months postoperatively. (20)

CVR increased after the endarterectomy, both ipsi and contralateral in 7 days, 2 and 4 months after, returning to normal values compared to pre-interventional where the CVR value was pathologically more affected contralateral, having slightly better values ipsilateral stenosis and approximately equal ones in 2 and 4 months after. This was due to the presence of contralateral carotid occlusion, representing an overall improvement of cerebral perfusion. Similar results were reported post-CAS. (16)

CONCLUSIONS

CT Cerebral Perfusion is useful to quantify the reduction of cerebral perfusion in patients with tight stenoses or with occlusions of the major cerebral arteries, the perfusion parameters alteration was correlated with the risk of hemodynamic infraction in the territory of stenotic artery. (6). The patients presented multiple cardiovascular risk factors, the cerebral hypoperfusion was more evident in the right hemisphere and due to the right carotid occlusion. The discovery and the treatment in due time of left carotid stenosis allowed the gradual restoration of cerebral perfusion in the left cerebral hemisphere (the patient also had a moderate vertebral artery stenosis) and the improvement of cerebral perfusion in right hemisphere.Thus MTT, CBV and CBF are increased in the case of pacients presenting significantlly severe stenosis of the carotid artery (demonstrated through angiography or US-chart) as well as in the case of an effective collateral circulation, and especially in the case of inefficient collateral, the increased values of MTT indicate a more imminent hemodynamic infarction (6).

Breath holding index is a useful method, easy to reproduce and use in real-time, to monitor the patients suffering from severe carotid stenosis. It is very useful for problems related to intracranial collateral circulation changes, insufficient hemodynamics and cerebrovascular stroke. (20) CVR is an important risk factor for strokes and TIA in patients with severe carotid stenosis, where the need for intervention is very important in order to improve the global cerebral perfusion. (21)

Both MFV-BHT and IP are important markers of cerebral hemodynamics and the study of CVR before CEA may be useful in identifying patients at risk for periprocedural complications and monitoring the patients through CVR calculation post-intervention can be useful to prevent subsequent cerebral ischemia. A meta-analysis revealed the fact that the CVR is associated with an increased risk of ischemic events in patients with carotid stenosis and may be useful for stroke risk stratification (21).

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