CEREBRAL HEMODYNAMIC CHANGES IN PATIENTS WITH SEVERE CAROTID STENOSIS PRE AND POST CEA OR CAS MONITORED THROUGH TCD

Marius Militaru[1,2], Anda Militaru[3], Stanca Ples[4,5], Raoul Pop[2,4], Mihaela Simu[2,4], Daniel Lighezan[1,2]

[1]Municipal Emergency Hospital, Timisoara
[2]University of Medicine and Pharmacy "Victor Babes", Timisoara
[3]Institute of Cardiovascular Diseases, Timisoara
[4]Emergency County Hospital, Timisoara
[5]Neuromed, Timisoara

ABSTRACT

Purpose. We have tried to emphasize the hemodynamic changes that occur in patients who experience uni/bilateral symptomatic/ asymptomatic severe carotid stenosis with acute or chronic ischemic stroke pre and post interventional (endarterectomy / stent) using TCD (Transcranian Doppler ultrasound) to determine BHT(breath holding test) and CVR (cerebrovascular reactivity) calculation.

Material and methods. 30 patients with severe carotid stenosis over 70% have been evaluated for the following endarterectomy (CEA) or stent placement (CAS). The Transcranial Doppler (TCD) was performed prior to surgery, at 72 hours and at 2 months after the intervention. Average flow velocities at middle cerebral artery (MCA) and pulsatility index (PI) ipsi/contralateral stenosis were recorded. CVR through the apnea test (BHT) was measured, recording an increase in the mean flow velocity and calculating MCA-BHI (breath-holding index) of ipsi and contralateral stenosis.

Results. Mean flow velocities (MFV) in the middle cerebral artery (MCA) have significantly increased both ipsilateral to stenosis from 31.01 + /-5.81cm / s prior to surgery, from 40.75 + /-7.53 cm / s (p <0.01) at 72 hours postCEA / CAS, as well as contralateral to stenosis, from 36.09 + / -6.49 before surgery to 42.31 + / -7.50 postintervention, and pulsatility index (PI) significantly increased ipsilateral from 0.72 + / -0.15 to 0.88 + / -0.12. (p <0.01) after both endarterectomy and after angioplasty and contralateral stent placement from 0.79 + / -0.16 to 0.97 + / -0.13 (p <0.01) in both postintervention studies (CEA / CAS) compared with presurgery carotid stenosis values. Mean flow velocities at MCA increased significantly 2 months after surgery both by CEA / CAS, with slightly better contralateral to carotid stenosis and after CAS. CVR (% / s) significantly increased statistically from 0.60 + / -0.58 to 0.85 + / -0.54 (p <0.05) postintervention, both at 72 hours postsurgery, and 2 months after surgery, both ipsi and contralateral to stenosis, both after endarterectomy and after stent.

Conclusions. Both endarterectomy and angioplasty with stent placement are interventional methods that produce significant increases in mean flow velocities in the MCA immediately after surgery, with improved cerebral parameters and cerebrovascular reactivity both ipsi and contralateral to stenosis right after surgery, but especially at 2 months after surgery. CVR had a significant statistical increase after endarterectomy or stent, with no difference between 72 hours and 2 months post intervention at ipsilateral and contralateral increases were significant, but with higher values at 72 hours (p <0.01) compared to 2 months (p <0.05), with slightly better ipsilateral to carotid stenosis at 2 month, regardless of the carotid atheromatosis degree contralateral to severe carotid stenosis.

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

INTRODUCTION

Carotid atheromatosis is one of the main causes of ischemic stroke. About 25%-30% of all cerebral ischemic events are caused by large vessel atherosclerosis, meaning changes in arterial wall at the big vessels, extra and intracranial (1). Carotid atheromatosis may cause cerebral ischemia by two mechanisms: thromboembolism (arterio-arterial embolism) and blood flow reduction (because of

Author for correspondence:
Marius Militaru, MD, Municipal Emergency Hospital,1-3, Sf Rozalia,Timisoara, Romania
e-mail: mili20m@yahoo.com

hemodynamics)(2). The obstruction of a vessel in the distribution territory of the carotid artery determines the infarction of a cerebral territory whose dimensions depend on the size of the obstructed vessel. The obstructive material may be a fragment of atheromatous plaques or arterial thrombus that detaches and migrates.(3) A severe carotid stenosis (of at least 70%) is needed to produce narrowing of the arterial lumen with decreased blood flow distal to the stenosis. In compensation, there is an expansion in arterial territory leading to impaired cerebral vasomotor reactivity (4).

Carotid artery stenosis may cause a stroke by both mechanisms; this is evidenced both by Transcranial Doppler Ultrasonography and MRI techniques (5). Large vessel atherosclerosis can cause almost any clinical syndrome of stroke, from asymptomatic arterial disease to TIA and ischemic stroke of varied severity in anterior and posterior circulation. (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).

European and American randomized controlled trials have demonstrated that carotid endarterectomy is the surgery to be performed at patients with symptomatic carotid stenosis over 70%,(11) and performed in patients with asymptomatic carotid stenosis over 70% as long as the stroke risk of perioperative stroke and death rate is less than 3 % and life expectancy of the patient is more than 5 years(12). Carotid stenting is a recently developed method compared to EAC, being considered an alternative to EAC in centers with a large number of procedures where documented mortality or stroke rate is below 6% in patients with symptomatic carotid stenosis above 70% and below 3 % in patients with asymptomatic severe carotid stenosis (13).

The aim of the study was to determine the effects of endarterectomy or stent on cerebral hemodynamics as a concequence of cerebral hemodynamic changes by measuring the mean flow velocities at MCA level and pulsatility index with TCD and the study of CVR by performing BHT, both before and immediately and at 2 months post intervention and the correlation with risk factors and the stroke.

METHODS

Patients and technique

30 patients (23 men, 7 women) were included in the study aged (62.5 + / -10.3), 7 women aged 67.1 + / -10 and 23 men aged 61.1 + / -10 with cardiovascular risk factors who presented with chronic, acute ischemic strokes, carotid TIA, lacunar ictuses, with severe carotidine stenosis, symptomatic / asymptomatic, unilateral / bilateral, which were framed for surgery (endarterectomy / carotid stenting) followed for 24 months. The degree of carotid stenosis was measured according to the criteria NASCET (North American Symtomatic Carotid Endarterectomy Trial) and patients with symptomatic carotid stenosis / asymptomatic over 70% were assessed.

41 patients were evaluated who presented more than 70% carotid stenosis, but 6 of the patients did not have adequate temporal bone window suitable for measurements on velocity of MCA, 3 patients could not be followed after surgery, and 2 patients had simultaneous moderate stenosis of MCA.

Patients had an acute cerebrovascular event in the anterior circulation ipsilateral to stenosis or had a ischemic stroke before admission to hospital or were found accidentally, being evaluated in 2011 – 2013. 21 (70%) symptomatic patients were included in the study and 9 (30%) asymptomatic patients, of which 6 (20%) patients with reduced CVR prior to intervention and 3 (10%) patients had contralateral to stenosis previous surgery: 2 CEA and 1 CAS.

Examination for inclusion tracked medical history, neurological status, ExtracranianDoppler / TranscranianDoppler, cerebral CT, EKG, laboratory tests, Angio CT cervical region, some patients performed brain MRI and Angiography four vessels. Carotid stenosis was assessed by ECD and confirmed by AngioCT. Cerebral CT was performed at all patients, 19 (63.3%) had cerebral MRI and 6 (31.5%) of those who performed endarterectomy were angiographicly evaluated.

17 (56.7%) of patients had a major stroke (rankin> 2), 7 (23.3%) minor stroke, 6 (20%) patients TIA (including amaurozis fugax), 1 patient presented in the therapeutic window had thrombolysis performed with favorable outcome being later stented, 17 (56.7%) had lacunar infarcts and 14 (46.7%) had chronic stroke (Table 1).

Demographic data on age, sex, risk factors, contralateral atheromatosis, type of intervention and type of ischemia prior to surgery are shown in Table 1.

The following were evaluated: blood pressure, cardiac and neurological symptoms classified as TIA, minor stroke, major stroke, symptoms of hyperperfusion (headache, confusion, increased arterial preassure) immediately after surgery and then every 2 months. Patients subsequently received aspirin 75 mg/day and clopidogrel 75 mg/day.

Transcranian Doppler Imaging

Cerebrovascular reactivity was evaluated through the BHT on ipsilateral MCA and contralateral to carotid stenosis, which is a predictive factor for patient tracking before and after surgery (endarterectomy / stent) on the risk of recurrent stroke and changes in cerebral hemodynamic parameters in response to control cerebral perfusion in relation to risk factors and previous cerebral event. (4)

Patients were followed pre surgery, to detect lesions and the day prior to surgery (maximum period is 2 weeks) and 3 days post surgery, two months post surgery with cerebral hemodynamics monitor-

TABLE 1. *Patient demographic date, vascular risk factors, type of intervention, type of ischemia before intervention and contralateral atheromatosis*

	No. of patients	%
Sex		
male	23	76.7
female	7	23.3
Vascular risk factors		
Hypertension	27	90
Diabetes mellitus	10	33.3
Hyperlipemie	24	80
Smoke	19	63.3
Pheriperal arterial disease	6	20
Obesity	8	26.7
Coronary disease	15	50
Type of ischemia before CEA/CAS		
TIA	6	20
Minor stroke	7	23.3
Major stroke(rankin>2)	17	56.7
Asymptomatic	9	30
Facial paresis	22	73.3
Hemiparesis	23	76.7
Motor afasia	10	33.3
Lacunar stroke	17	56.7
Sechelar stroke	14	46.7
Type of intervention		
CEA	19	63.3
CAS	11	36.7
Concomitent contralateral atheromatosis		
Contralateral ICAstenosis	9	30
50%-70%	8	26.7
70%-99%	1	3.3
Contralateral ICA occlusion	5	16.7
Vertebral artery stenosis	4	13.3
Subclavia artery stenosis	6	30
Contralateral carotid ateromatosis	18	60

Note*: ICA – internal carotid artery;CAS – carotid angioplasty stent; CEA carotid endarterectomy; TIA – transitory ischemic attack.*

ing by TCD with RCV 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 pricedure, 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)

Statistic analysis

For statistical analysis SPSS program was used version 20.0, the results are expressed in percentages, mean + /-standard deviation. Hemodynamic changes of MCV, IP, CVR before and after surgery were evaluated through Test T-pair, differences in values between symptomatic and non symptomatic values were assessed with the test T independently.A value of * p <0.01, ** p <0.05 was considered statistically significant.

RESULTS

The carotid artery damage of over 70% was equal: 15 (50%) patients with right ACI stenosis and 15 patients (50%) with left ACI stenosis, 15 (50%) patients had stenoses ranging from 70% -89% and 15 (50%) patients had ACI stenosis between 90% – 99% of which 8 (26.7%) patients had stenosis preocluzive about 95-99%. 19 (63.3%) patients had endarterectomy, 11 (36.7%) patients had angioplasty with stent, and 3 (10%) patients had previous contralateral surgery.

18 (60%) patients had contralateral carotid atheromatosis, 9 (30%) patients contralateral carotid stenosis over 50% of which 8 (26.7%) patients with stenosis between 50% -70% and 1 (3.3%) patients with stenosis between 70% -99%, 5 (16.7%) patients with contralateral occlusion, 4 (13.3%) patients with vetebral stenosis and 6 (30%) patients with subclavian artery stenosis. There weren't any deaths recorded after surgery, major stroke or heart attack. 6 (20%) patients of which 4 (13.3%) after stent and 2 (6.7%) after endarterectomy (presented symptoms were considered HPS(hyperperfusion) immediately after surgery: 2 (6.7%) headache, 3 (10%) high blood pressure and 1(3.3%) patient with mild confusion, symptoms gone after 24 hours.

After surgery, ipsilateral to stenosis TCD showed a significant increase of MFV from 31.01 + /-5.81cm / s prior to surgery to 40.75 + /-7.53 cm / s (p <0.01) and IP increased from 0.72 + / -0.15 to 0.88 + / -0.12. (p <0.01). Contralateral stenosis revealed as both significant increase of MFV increase from 36.09 + / -6.49 before surgery to 42.31 + / -7.50, and the IP of 0.79 + / -0.16 to 0.97 + / -0.13 (p <0.01). (Table 2)

At 2 months after surgery ipsilateral to stenosis there was an increase in MFV to 42.61 + / -7.82 and IP 1.01 + / -0.13, contralateral to stenosis from 45.79 + / -8.19, IP at 1.07 + / -0.12, and compared to the values of MFV and IP pre surgery there was a significant increase (p <0.01). (Table 2)

Whatever type of intervention used, after both endarterectomy and after stent placement there were significant increases in both the IP and MFV, both ipsi and contralateral to stenosis with slight better values contralateral to stenosis, at stent patients: MFV ipsilateral to stenosis increased from 31.92 + / -7.37 preCAS to 41.64 + / -8.59 postCAS and MFV ipsilateral to stenosis increased from 30.48 + / -4.83 preCEA at 40.24 + / -7.04 postCEA p <0.01 (Table 3). After 2 months from the intervention the same significant increase was observed in MFV and IP after both endarterectomy and stent, both ipsi and contralateral to severe stenosis with slightly better values after angioplasty with stent p <0.01 (Table 3).

After the apnea test (BHT) was done as well as after the endarterectomy and after the stent placement, an increase of the average flow velocity was

***TABLE 2.** Hemodynamic changes immediately after intervention (72 h) – POST 1 and 1-2 month later – POST 2 compared with pre-intervention (CEA/CAS) and p values (statistical significance)*

DOPPLER values normal	IPSILATERAL			CONTRALATERAL		
MCA	PRE CEA/ CAS	POST 1 CEA/CAS	POST 2 CEA/CAS	PRE CEA/CAS	POST1 CEA/CAS	POST2 CEA/CAS
MFV	31.01+/-5.91	40.75+/-7.53*	42.61+/-7.82*	36.09+/-6.49	42.31+/-7.50*	45.79+/-8.19*
IP	0.72+/-0.15	0.88+/-0.12*	1.01+/-0.13*	0.79+/-0.16	0.97+/-0.13*	1.07+/-0.12*

*Note: MCA – middle cerebral artery; MFV – mean flow velocity; IP – pulsatility index, CEA – carotid endarterectomy; CAS – carotid angioplasty stent; POST1 – 72h after intervention; POST2 – 2 month later; * P<0.01;*

***TABLE 3.** Compared hemodynamic changes between CEA and CAS (72 h) – POST 1 and 1-2 month later – POST 2 compared with pre CEA/CAS and p values (statistical significance)*

DOPPLER values normal	IPSILATERAL		CONTRALATERAL	
MCA	MFV	IP	MFV	IP
PRECEA	30.48+/-4.83	0.72+/-0.15	35.03+/-4.61	0.77+/-0.14
PRECAS	31.92+/-7.37	0.72+/-0.15	37.93+/-8.82	0.82+/-0.19
POST1CEA	40.24+/-7.04*	0.91+/-0.12*	40.68+/-5.76*	0.95+/-0.13*
POST1CAS	41.64+/-8.59*	0.84+/-0.12*	45.12+/-9.47*	1.00+/-0.15*
POST2CEA	42.13+/-7.34*	1.01+/-0.13*	43.94+/-6.86*	1.05+/-0.13*
POST2CAS	43.64+/-8.89*	1.00+/-0.13*	49.00+/-9.60*	1.09+/-0.11*

*Note: MCA – middle cerebral artery; MFV – mean flow velocity; IP – pulsatility index, CEA – carotid endarterectomy; CAS – carotid angioplasty stent; POST1 – 72h after intervention; POST 2 – 2 month later; * P<0.01;*

***TABLE 4.** Hemodynamic changes after BHT between CEA and CAS (72 h) – POST 1 and 2 month later – POST 2 compared with pre CEA/CAS and p values (statistical significance)*

DOPPLER values	IPSILATERAL			CONTRALATERAL		
MCA	PRE CEA/CAS	POST 1 CEA/CAS	POST 2 CEA/ CAS	PRE CEA/CAS	POST1 CEA/CAS	POST2 CEA/CAS
MFV normal	31.01+/-5.91	40.75+/-7.53	42.61+/-7.82	36.09+/-6.49	42.31+/-7.50	45.79+/-8.19
BHT-MFV	36.43+/-7.82*	50.61+/-7.15*	52.66+/-6.87*	41.69+/-7.19*	53.04+/-7.59*	55.60+/-8.32*
BHT-CEA	35.71+/-6.93	49.48+/-7.31	51.70+/-6.96	39.87+/-6.00	50.88+/-6.38	53.58+/-7.19
BHT-CAS	37.67+/-9.40	52.55+/-6.76	54.31+/-6.71	44.83+/-10.17	56.76+/-8.36	59.09+/-9.30
CVR(%/s)	0.60+/-0.58	0.85+/-0.54**	0.84+/-0.54**	0.53+/-0.53	0.88+/-0.47*	0.74+/-0.45**

*Note: MCA – middle cerebral artery; MFV – mean flow velocity; BHT – breath-holding test; CEA – carotid endarterectomy; CAS – carotid angioplasty stent; POST1 – 72h after intervention; POST 2 –2 month later; RCV – cerebrovascular reserve *P<0.01;**p<0.05*

observed immediately after surgery and also after 2 months, both ipsilateral and contralateral, with slight higher values after angioplasty with stent placement.(Table 4);

MFV increased significantly from 31.01 + / -5.91 after a normal breathing to 36.43 + / -7.82 after BHT pre-interventional of ipsilateral stenosis, (p <0.01) and also the contralateral stenosis from 36.09 + / -6.49 to 41.69 + / -7.19 pre-interventional (p <0.01). Cerebral hemodynamic changes were observed 72 hours post-intervention through a significant increase of the MFV values from 40.75 + / -7.53 to 50.61 + / -7.15 p <0.01, and especially after 2 months post-intervention from 42.61 + / -7.82 to 52.66 + / -6.87 (p <0.01) of ipsilateral stenosis (table4). The cerebral hemodynamic changes, through a significant increase of the average flow velocities at MCA level, were slightly better of contralateral stenosis 2 months post-intervention from 45.79 + / -8.19 to 55.60 + / -8.32 (p <0.01) (Table 4).

The pre-interventional CVR was normal in 13 patients (43.3%) and pathological in 17 (56.7%) both ispilateral and contralateral stenosis, and 21 patients (70%) had pathological RCV both ipsilateral and contralateral stenosis.

Post-intervention, the CVR has improved after 72 hours, ipsilateral, 24 (80%) patients had normal CVR, an increased value comparing to the pre-intervention one, while 6 (20%) patients had a pathological one and contralateral 23 (76.7 %) patients had normal CVR and 7 (23.3%) pathological and 9 (70%) patients had pathological CVR both ipsilateral and contralateral stenosis, these changes were emphasized regardless of the previous CVR value (normal or pathological).

After 2 months from the intervention,7 (23.3%) ipsilateral patients and 8 (26.7%) contralateral patients had pathological RCV, 19 (63.3%) patients had normal RCV and 11 (36.7%) patients had pathological RCV both ipsilateral and contralateral severe stenosis.

RCV (% / s) increased significantly after the endarterectomy or stent from 0.60 + / -0.58 to 0.85 + / -0.54 (p <0.05) showing no differences between the 72 hours and the 2 months post-intervention ipsilateral, and contralateral the increases were significant but presenting higher values 72 hours later (p <0.01) comparing to 2 months (p <0.05) (Table 4). Comparing the 21 symptomatic patients and the 9 asymptomatic regarding the MFV(normal), IP, MFV BHT and RCV there were not highlighted statistically significant values (p> 0.05) ipsilateral, contralateral, nor pre-intervention or post-intervention 72 hours later respectively 2 months and also the type of intervention was not influenced, endarterectomy or sent (p> 0.05). (See fig 1. 2).

There were no statistically significant changes of MFV, IP, CVR or of symptomatic / asymptomatic patients who had / no (27/3) contralateral intervention (CEA / CAS) prior to the event.

In patients with symptomatic stenosis (21) out of which 8 stent and 13 endarterectomy, it was highlighted a significant increase in MFV, IP, MFV-BHT 72 hours later and as well as 2 months after

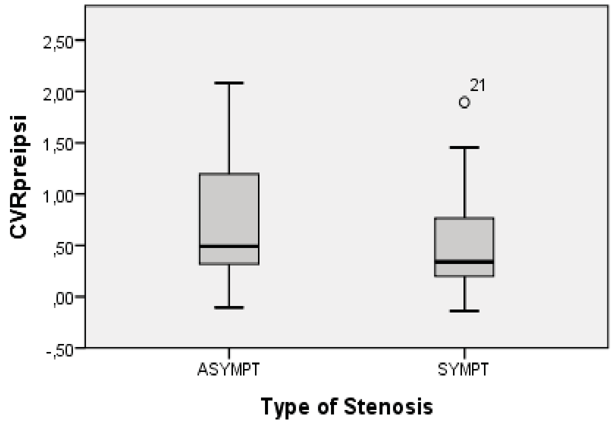

FIGURE 1. *CVR pre-intervention ipsilateral according to the type of stenosis*

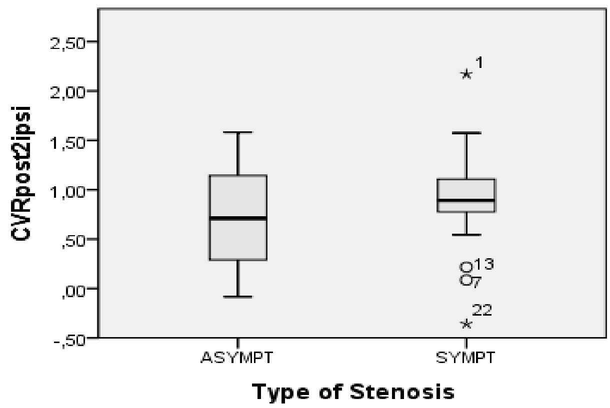

FIGURE 2. *CVR 2 months post-intervention ospilateral according to the type of stenosis*

the endarterectomy or stent p <0.01, with better values of ipsilateral stenosis, as well as the CVR p <0.05 with slightly better values in 72 hours post-intervention p <0.01 and ipsilateral stenosis (see table 4, 5), without significant changes between the two types of interventions (MFVpre-intervention CAS 28.84+/-6.09 respectively CEA 31.23+/-3.92 and MFV post-intervention CAS 39.93+/-6.61respectively CEA 41.79+/-6.88; MFV-BHT pre-in-

TABLE 5. *Hemodynamic changes 2 months post-intervention compared with pre-intervention (CEA/CAS) at different type of stenosis and p values (statistical significance)*

Doppler value	TYPE OF STENOSIS	ipsilateral		contralateral	
MCA		PRE CAS/CEA	POST CAS/CEA	PRE CAS/CEA	POST CAS/CEA
MFV-normal	symptomatic	30.32+/-4.87	41.08+/-6.67*	35.32+/-6.20*	45.73+/-8.63*
	asymtomatic	32.62+/-7.67	46.18+/-9.47	37.88+/-7.17	45.93+/-7.55
MFV-BHT	symptomatic	35.24+/-6.51	51.71+/-6.72*	40.30+/-7,66*	55.90+/-8.97
	asymtomatic	39.20+/-10.17	54.85+/-7.11	44.94+/-8.24	54.91+/-6.98
CVR	symptomatic	0.55+/-0.54	0.90+/-0.54**	0.49+/-0.56	0.78+/-0.50**
	asymtomatic	0.70+/-0.67	0.70+/-0.57	0.63+/-0.45	0.67+/-0.28

Note: MCA – middle cerebral artery; MFV – mean flow velocity; BHT – reath-holding test; CEA – carotid endarterectomy; CAS – carotid angioplasty stent; CVR-cerebrovascular reserve;
** P<0.01 **p<0.05*

tervention CAS 34.03+/-7.02, respectively CEA 35.99+/-6.35, and post-intervention CAS-53.08+/-5.78, respectively CEA 50.87+/-7.33).For the 9 asymptomatic patients it was observed an increase of the normal MFV, MFV- BHT post-interventional had better ipsilateral values than contralateral and CVR value had no significant changes of ipsilateral stenosis 2 months after the intervention, having a slight increase in contralateral stenosis after 2 months. (Table 5).

DISCUSSION

Regarding the risk factors, it was emphasized that, the hemodynamic changes were highlighted post-intervention not only after endarterectomy but also after angioplasty with stent, both ipsilateral and contralateral severe carotid stenosis. 27 of the patients had HTA out of which 10 had CAS and 17 CEA, MFV increased from 30.91 + / -6.12 pre-intervention to 40.88 + / -7.93 72 hours post-intervention and after BHT, MFV increased from 36.15 + /-8.14 pre-intervention to 50.61 + / -7.55 post-intervention, having no changes of the type of intervention (CEA / CAS).

Regarding the ischemic cerebral events there were 17 (56.7%) patients with major stroke (ranking> 2), out of which 13 (76.5%) were men and 4 (23.5%) women with ipsilateral CVR, pre-intervention 0.70 + / -0.68 which significantly increased (p <0.01) post-intervention after 2 months to 0.92 + / -0.47, but with no significant changes in 72 hours post-intervention. The contralateral CVR significantly increased statistically (p <0.05) from 0.47 + / -0.52 pre- intervention from 0.77 + / -0.46 2 months post-intervention. 11 (64.7%) patients with major stroke had pathological CVR ipsilateral (<0.5% / s), and 6 (35.3%) patients had normal CVR(> 0.5% / s) and contralateral pre-intervention, 9 (52.9%) patients had pathological CVR. 72 hours post-intervention regarding both ipsilateral and contralateral, there were 15 (88.2%) patients with normal CVR and only 2 (%) patients with pathological CVR and 2 months post-intervention ipsilateral / contralateral there were 2 (11.8%) / 4 (23.5 %) patients with pathological CVR respectively 15 (88.2%) / 13 (76.5%) patients had normal CVR, all these representing a very good improvement of the normal CVR value 72 hours and 2 months post-intervention.

12 patients had carotid TIA including amaurozis fugax out of which 6 were men and 6 were women. The CVR values increased but not statistically significant: ipsilateral from 0.61 + / -0.60 to 0.82 + / -0.43 72 hours later and 0.87 + / -0.51 2 months later and contralateral increased, but not statistically significant from 0.57 + / -0.46 to 0.82 + / -0.49 72 hours later and decreased slightly to 0.66 + / -0.42 2 months post-intervention. Before the intervention there were 6 (50%) ipsilateral patients and 8 (66.7%) contralateral patients with pathological CVR, the CVR significantly improved in 72 hours post-intervention remaining with only 2 (16.7%) / 3 (25%) patients ipsilateral / contralateral with pathological CVR and 10 (83.3%) / 9 (75%) patients with normal CVR.

In this study the effects of cerebral hemodynamics were assessed by CAS / CEA, the TCD showed a significant increase of MFV in both ipsilateral and contralateral after the intervention, this can be analyzed through the increase of the perfusion pressure as a consequence returning to the normal diameter and flow ACI after CEA / CAS. Similar results were reported after CAS (14) or CEA (15). We observed increase of MFV contralateral stenosis 72 hours later and in 2 months post CAS / CEA. Similar results were reported after CEA (16). In other studies (17,18) there were not observed significant increases contralateral, while other studies showed a moderate increase contralateral as a consequence of the collateral flow through the interior communicating artery after CEA (19,20). Other studies that observed the CEA (21) showed that the lack of increase of contralateral MFV post-intervention was due to the presence of severe stenosis and contralateral chronic hypoperfusion. In our study, 9 (30%) patients had stenoses> 50% contralateral ACI (8 (26,7%) had stenoses between 50-70% and 1 (3,3%) had stenoses>70%), 5 (16.7%) contralateral ACI occlusion and 18 (60%) contralateral carotid atheromatosis.

In this study the IP increased bilaterally post-intervention, this representing the vasoconstriction ability of the arteriolar resistance to maintain a significant increase of the flow within the ACI after CEA / CAS. Similar results have been reported post CAS (14). In a study that observed 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 through an increase of the IP (16). Another study that observed patients with CEA, revealed that the IP is a better predictor for the risk of hyperemia and stroke during and after the intervention (21,22). There were also reported cases in which the patients presented headaches and HTA after the CEA and a decrease of MFV and IP was observed after CEA, and this was interpreted as a refractory vasodilatation due to the RCV response to high perfusion pressure after recanalization of ACI (23). In this study there were 2 (6.7%) patients with headaches, 3 (10%) patients with hypertension and 1 (3.3%) patient with mild confusion, delivered after 24 hours postoperatively, who showed slightly higher values of the postoperative IP to those who had no headaches or hypertension.

There were no deaths, major strokes or heart attacks. None of the patients had TIA or strokes immediately after CAS / CEA.

At 2 months post-intervention the increase of MFV compared to the values pre-intervention were maintained compared to those of 72 hours later, with slightly better values of contralateral stenosis and those with CAS, this indicated an improvement in cerebral perfusion. IP increased after 2 months compared to the initial value in both hemispheres, with slightly better values after CAS(14).Similar results were observed after CAS (14,24). Another study showed an increased MFV and IP with statistically significant values ipslateral stenosis, due to the vasoconstriction of the arteriolar resistance regarding the hyperemia as a response to unilateral perfusion and to the unilateral rehabilitation of self-regulation mechanism (17). Another study that observed patients after CEA reported similar results, with an improvement and normalization of cerebral parameters for patients that were observed up 3 to 12 months postoperatively. (25,26,27)

The CVR increased statistically significant after both endarterectomy and stent, both ipsi and contralateral 72 hours and 2 months post-intervention, with slightly better values 72 hours later and contralateral,and slightly better values 2 month later and ipsilateral, representing an overall improvement of cerebral perfusion, and another study showed similar results with an increase of the CVR post-intervention with slightly better values of ipsilateral stenosis. (17)

CONCLUSIONS

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.

The endarterectomy and the angioplasty with stent improved global cerebral perfusion and CVR as TCD values indicated. Within 72 hours from intervention it was emphasized an improvement of the MFV, IP, CVR in most patients regarding the adjusting of the cerebral perfusion through the ability of cerebral arterioles to have vasoconstriction in order to maintain a constant cerebral blood flow. These hemodynamic changes are also maintained two months after the intervention, with slight increases of the contralateral compared to ipsilateral and the CVR increased statistically significant post- intervention having a slight increase 72 hours later, with slight increases of the ipsilateral compared to contralateral after 2 month. There were no statistically significant changes for the symptomatic and asymptomatic patients or for the type of intervention, endarterectomy or stent. Similar results were observed after CAS (24).

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 issues related to intracranial collateral circulation changes, insufficient hemodynamics and cerebrovascular stroke. (25)

Both MFV-BHT and IP are important markers of cerebral hemodynamics and the study of CVR before CAS / 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 (28).

REFERENCES

1. **J.P. Mohr and Jean Claude Gautier** – Stroke (Fourth Edition), Pathophysiology, Diagnosis, and Management, Chapter 5, *Internal Carotid Artery Disease,* 2001; 75-100
2. **Martin A. Samuels, Allan H. Ropper** – Samuels"s Manual of Neurologic Therapeutics, *Stroke and cerebrovascular disorders*, Eight Edition 2010; 373-394
3. **Mark Mumenthaler, Heirich Mattle** – Neurology, *Disturbance of Cerebral Perfusion*, 4th edition, 2004; 131-209
4. **Cristina Tiu** – Neurosonology,Carotid Stenosis,100-129, *Cerebrovascular reactivity*, 2006; 217-231
5. **Bornstein N.M.** – Stroke, Practical guides for clinicians, Classification of Stroke subtypes, *Karger* 2009; 50-63
6. **Claire L.Allen, Ulvi Bayraktutan** – Risk factors for ischemic stroke, *International Journal of stroke,* may 2008, vol 3, 105-1162
7. **E.W. Baumgartner** – Handbook of Neurovascular Ultrasound, Atherosclerotic Carotid Stenosis and Occlusion, 2006; pp 36-56
8. Zsolt Gorani, Andrei V. Alexandrov – Neurosonology, Neurology Clinics 2008; 89-108
9. **Stoll, Martin Seidel, Antje; Treib, Johannes** – Influence of Different Techniques of Breath Holding on the Measurement of Cerebrovascular Reserve in Carotid Artery Disease, *Stroke A Journal of Cerebral Circulation,* Volume 27(6) June 1996; pp 1132-1133
10. **Andrei V. Aexandrov** – Cerebrovascular Ultrasound in stroke prevention and treatment, Fenwick T., *TCD and sickle cell disease*, 133-147
11. **Joseph F. Pola** – Cardiovascular risk factors and carotid ultrasound, 2004; 148-160

12. **North American Symptomatic Carotid Endarterectomy Trial Collaborators** – Beneficial effects of carotid endarterectomy in symptomatic patients with high grade carotid stenosis. *N Engl J Med* 1991; 325:445–53
13. **European Society of Cardiology** – Guidelines on the diagnosis and treatment of peripheral artery diseases, *European Heart Journal* 2011; 32:2851-2906
14. A randomised trial, Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS). *Lancet* 2001; 357:1729-37
15. **Giorgos Sfyroeras, Christos D. Karkos, Charalampos Liasidis** – The impact of carotid stenting on the hemodynamic parameters and cerebrovascular reactivity of the ipsilateral middle cerebral artery. *J Vasc Surg.* 2006 Nov; 44(5):1016-22
16. **Muller M., Behnke S., Walter P.** – Cerebrovascular resistance and blood flow velocity changes after carotid endarterectomy. *Vascular Disease*, 1999; 28:279-82
17. **Zachrisson H., Blomstrand C., Holm J., et al.** – Changes in middle cerebral artery blood flow after carotid endarterectomy as monitored by transcranial Doppler. *J Vasc Surg* 2002; 36:285-90
18. **Sanchez-Arjona M.B., G. Sanz-Fernández** – Cerebral Hemodynamic Changes after Carotid Angioplasty and,2007, *Am J Neuroradiol.* 2007 Apr; 28(4):640-4
19. **Blohme L., Pagani M., Parra-Hoyos H., et al.** – Changes in middle cerebral artery flow velocity and pulsatility index after carotid endarterectomy. *Eur J Vasc Surg* 1991; 5:659-63
20. **Araki C.T., Babikian V.L., Cantelmo N.L., et al.** – Cerebrovascular hemodynamic changes associated with carotid endarterectomy. *J Vasc Surg* 1991; 13:854-59
21. **Maltezos C.K., Papanas N. et al** – Changes in blood flow of anterior and middle cerebral arteries following carotid endarterectomy: a transcranian Doppler study. *Vasc Endovasc Urg* 2007 oct-nov; 41(5)389-96
22. **Naylor A.R., Whyman M.R., Wildsmith J.A., et al.** – Factors influencing the hyperaemic response after carotid endarterectomy. *Br J Surg* 1993; 80:1523-27
23. **Enevoldsen E.M., Norby J., Rohr N., et al.** – Outcome for patients with carotid stenosis undergoing carotid endarterectomy, the cerebral condition followed by extra/intracranial ultrasound examinations. *Acta Neurol Scand* 1999; 99:340-48
24. **Gil-Peralta A., Mayol A., Marcos J.R., et al.** – Percutaneous transluminal angioplasty of the symptomatic atherosclerotic carotid arteries. Results, complications, and follow-up. *Stroke* 1996; 27:2271-73
25. **Brcic I., Horner S., Thaler D.** – Improved cerebral Vasoreactivity following Percutaneous Transluminal Angioplasty with Stenting of High Grade Internal carotid Artery stenosis, *Cerebrovascular Disease*, vol 25, no 6, 2008; 555-560
26. **Zavoreo Iris, Lisak Marjana, Demarin Vida** – Correletion of neurological Symptoms and BHI values in patients with severe carotid stenosis, *Cerebrovascular disease*, 2005; 19, suppl 19:1015-9770
27. **Dalman J.E., Beenakkers I.C., Moll F.L.L., et al.** – Transcranial Doppler monitoring during carotid endarterectomy helps to identify patients at risk of postoperative hyperperfusion. *Eur J Vasc Endovasc Surg* 1999; 18:222-27
28. **Nielsen M.-Y., Sillesen H.H., Jorgensen L.G., et al.** – The haemodynamic effect of carotid endarterectomy. *Eur J Vasc Endovasc Surg* 2002; 24:53-58
29. **Gupta A., Chazen J.L., Hartman M., et al.** – Cerebrovascular reserve and stroke risk in patients with carotid stenosis or occlusion: a systematic review and meta-analysis. *Stroke*. 2012 Nov; 43(11):2884-91