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International Journal of
Cerebrovascular Disease and Stroke

Semenyutin VB, et al. Int J Cerebrovasc Dis Stroke 4: 139.

Research Article

DOI: 10.29011/2688-8734.000039

Cerebral Autoregulation and Blood Flow Redistribution in the Precerebral Arteries in Patients with Carotid Artery Occlusion

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Citation: Semenyutin VB, Nikiforova AA, Samochernykh KA (2021) Cerebral Autoregulation and Blood Flow Redistribution in the Precerebral Arteries in Patients with Carotid Artery Occlusion. Int J Cerebrovasc Dis Stroke 4: 139. DOI: 10.29011/2688-8734.000039

Received Date: 20 July, 2021; **Accepted Date:** 03 August, 2021; **Published Date:** 09 August, 2021

Abstract

Background: State of cerebral autoregulation and changed blood flow in the precerebral arteries can serve as selection criteria in favor of extra-intracranial bypass surgery and as a prediction factor in patients with carotid artery occlusion. However, information capacity of quantitative values of this functional state of the brain circulation has not been studied well enough.

Objective: The objective is to assess the state of cerebral autoregulation and blood flow redistribution in the precerebral arteries in patients with carotid artery occlusion.

Material and methods: The study involved 24 patients aged 41 to 80 with carotid artery occlusion. Eight of them were asymptomatic. We measured blood flow velocity in intracranial arteries by using transcranial Doppler (MultiDop X) and flow velocity index in precerebral arteries - by using duplex scanning (Vivid e). Cerebral autoregulation was evaluated with cross-spectral analysis of spontaneous oscillations of blood pressure (CNAP, Austria) and blood flow velocity within the range of Mayer's waves (80-120 mHz).

Results: In most symptomatic patients the cerebral autoregulation decreased on both sides (0.3±0.3 rad ipsilaterally and 0.6±0.4 rad contralaterally). There was no cerebral autoregulation impairment in all asymptomatic patients (1.1±0.5 rad ipsilateral and 1.3±0.5 rad contralateral). We noticed an increased blood flow index in the contralateral internal carotid artery (312±113 ml/min) and ipsilateral vertebral and external carotid arteries (126±64 ml/min and 158±72 ml/min, respectively).

Conclusions: A comprehensive analysis of cerebral autoregulation and blood flow in the precerebral arteries helps to identify the extent of cerebral hemodynamics compensation in carotid artery occlusion, which can classify patients in need of revascularization surgery.

Keywords: Blood flow index; Carotid artery occlusion; Cerebral autoregulation; Cerebrovascular reserve; Extra-intracranial bypass surgery

Introduction

Classification of patients with carotid artery occlusion for the purpose of pathogenetic and clinically sound selection in favor of extra-intracranial bypass surgery has long been a topical issue, since in the vast majority of carotid artery occlusion cases patients have sufficient compensation of cerebral hemodynamics through natural intracranial anastomoses of the contralateral carotid and vertebrobasilar basins, and through extra-intracranial collateral pathways of the External Carotid Artery (ECA) [1-3]. Obviously, activation of the collateral circulation due to carotid artery occlusion ensures cerebral perfusion pressure enough to meet the needs of the brain in the occluded artery region, which is why, indications for extra-intracranial bypass surgery are ambiguous. In this case, objective identification of a decreased Cerebrovascular Reserve (CVR) and a compensation stage of cerebral hemodynamics becomes a crucial matter [4-6].

Many researchers identify stages of hemodynamic failure of brain circulation relying upon comprehensive assessment of cerebral blood flow values. For instance, R. Grubb et al. [7], measured Oxygen extraction fraction and CVR by positron emission tomography to formulate three stages of hemodynamic failure in patients with carotid artery occlusion: during the first (compensated) stage, CVR decreases and Oxygen extraction fraction is not changed. During the second (subcompensated) stage, decreasing CVR is accompanied by increased Oxygen extraction fraction. During the third stage, Oxygen extraction fraction increases to maximum, and CVR is depleted, which is why this stage is considered as decompensated [7]. Some researchers believe that an increasing Oxygen extraction can serve as an independent predictor of ischemic stroke in patients with carotid artery occlusion [7-10].

Apparently, intensity of collateral circulation is a key factor in growth of hemodynamic impairment in the compromised region. It has been proved that results of precerebral blood flow assessment and the state of Cerebral Autoregulation (CA) can be used in order to optimize the surgical tactics and predict outcomes in patients with carotid artery stenosis [11]. However, the information content of these quantitative parameters of this functional state of the brain circulation in patients with carotid artery occlusion is determined to a lesser extent.

Objective

The objective is to assess the state of CA and blood flow redistribution in the precerebral arteries in patients with carotid artery occlusion.

Materials and Methods

The study involved 24 patients (19 men, 5 women) with carotid artery occlusion, with mean age of 60±9 (Table 1).

No.	Age (full years)	Sex	Type of Disease	mRs (degree)	Degree of Stenosis (%)		CoW Anatomy Variations
					c ICA	i VA	
1	48	m	S	1	50	–	I
2	64	m	S	1	91	42	I
3	59	m	S	1	51	–	I
4	61	m	S	4	54	–	VI
5	47	f	S	2	–	–	I
6	61	m	S	1	60	–	I
7	53	m	S	1	–	–	I
8	68	f	A	0	–	–	I
9	70	m	S	2	–	–	III
10	60	m	S	2	–	–	III
11	46	m	S	1	70	–	IV
12	80	m	A	1	–	–	I
13*	62	f	A	1	81	–	I
14	65	m	A	0	100	–	I
15	48	m	S	1	–	–	I
16	57	f	A	0	40	–	II
17	69	m	A	1	–	43	I
18	54	m	A	0	–	39	I
19*	67	f	S	0	–	–	III
20*	66	m	S	1	–	53	V
21	41	m	A	0	–	–	IV
22	66	m	S	2	–	–	I
23	61	m	S	2	–	–	I
24	58	m	S	2	44	–	IV

A: Asymptomatic; **S:** Symptomatic; **M:** Male; **F:** Female; **c ICA:** contralateral Internal Carotid Artery; **i VA:** ipsilateral Vertebral Artery; **mRs:** Modified Renkin scale; **CoW:** Circle of Willis; **I:** Complete; **II:** Absent the A1 segment contralateral anterior cerebral artery; **III:** Absent ipsilateral posterior communicating artery; **IV:** Absent contralateral posterior communicating artery; **V:** Absent ipsi- and contralateral posterior communicating arteries, **VI:** Absent anterior and ipsi- and contralateral posterior communicating arteries; *****: temporal acoustic window failure

Table 1: Characteristics of patients with carotid artery occlusion.

Carotid artery occlusion was proved by duplex scanning and by multi-slice computed or cerebral angiography. Eight patients were asymptomatic. Sixteen patients were symptomatic (early or late recovery period): 15 patients had ipsilateral ischemic stroke, 1 patient - ipsilateral transient ischemic attack. The study had no patients with acute carotid artery occlusion. Functional outcomes after stroke were assessed by the modified Renkin scale (mRs).

In order to assess the state of CA we monitored Blood Flow Velocity (BFV) by using transcranial Doppler in the cerebral arteries (MultiDop X DWL) and systemic Blood Pressure (BP) by digital photoplethysmography (CNAP). CA was evaluated with cross-spectral analysis of spontaneous oscillations of BP (CNAP, Austria) and BFV in both Middle Cerebral Arteries (MCA) within the range of Mayer's waves (80-120 mHz). We determined value of the Phase Shift (PS) between BFV and BP to identify the maximum amplitude of the M-waves of BP, with coherence of at least 0.6. When PS was <0.8 rad, the state of CA was impaired [12,13]. The Flow Velocity Index (FVI) in the precerebral arteries was determined by using duplex scanning (Vivid e) and calculated as the product of the cross-sectional area of each artery by the weighted mean BFV (time-averaged mean velocity TAMEAN) on the straight section, with Doppler angle no more than 60˚ [14,15]. Normal FVI values in the Internal Carotid Artery (ICA) were 170-280 ml/min, in Vertebral Artery (VA) - 35-120 ml/min, in ECA – 80-190 ml/min [16].

The data was statistically processed in the standard statistical software (Statistica 12.0 for Windows, Excel), using parametric (Student's) and non-parametric (Kolmogorov-Smirnov) criteria. P <0.05 was statistically significant.

The patients' screening protocol was approved by the Ethics Board of the Russian Polenov Neurosurgical Institute (Protocol No. 1 of 02.06.2010). All patients participating in the clinical study gave their written voluntary informed consent. The study complied with requirements of the Declaration of Helsinki of the World Medical Association.

Results

During transcranial Doppler, duplex scanning of the precerebral arteries and bilateral monitoring of BFV in the MCA no significant changes were detected in BP. Mean BP values were within the range 65-109 mm Hg (92±11 mm Hg).

Figure 1 shows a diagram of mean values of BFV in the arteries supplying blood to the brain and mean values FVI in precerebral arteries.

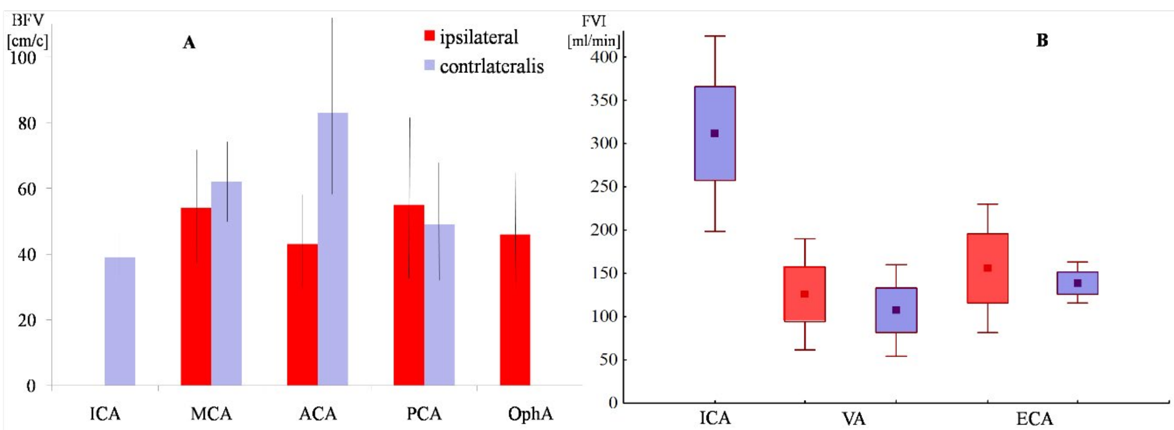

Figure 1: Mean values of Blood Flow Velocity (BFV) in the arteries supplying blood to the brain **(A)** and mean values of Flow Velocity Index (FVI) in the precerebral arteries **(B)** in patients with carotid artery occlusion. **ICA:** Internal Carotid Artery; **MCA:** Middle Cerebral Arteries; **ACA:** Anterior Cerebral Arteries; **PCA**: Posterior Cerebral Arteries; OphA: Ophthalmic Artery (in 13 patients with active anastomosis through the retrograde ophthalmic artery); **VA:** Vertebral Artery; **ECA:** External Carotid Arteries.

Transcranial Doppler

No significant asymmetry of BFV in MCA was detected (p>0.1). A significant (p<0.05) increase of BFV in the contralateral Anterior Cerebral Artery (ACA) and the ICA spoke for activated collateral circulation through the Anterior Communicating Artery (ACoA) of the Circle of Willis (CoW), which was detected in most patients. Also, most (n=14) patients had an increasing BFV in the ipsilateral Posterior Cerebral Artery (PCA); however, we found no significant difference with BFV in the contralateral PCA. 13 patients had active anastomosis through the retrograde ophthalmic artery with retrograde blood flow, an increased BFV and a decreased pulsation index in the ipsilateral ophthalmic artery. BFV in other intracranial arteries were within the age norm.

Flow Velocity Index in Precerebral Arteries

There was a significant (p<0.05) increase in FVI in the contralateral ICA (save for 6 patients with severe stenosis or absent ACoA of the CoW) and in the ipsilateral VA (save for 7 patients with stenosis or posterior communicating arteries (PCoA) of CoW). 8 patients had active anastomosis through the retrograde ophthalmic artery and an increased FVI in the ipsilateral ECA (in 5 patients it was not possible to identify FVI due to stenosis). FVI values were greatly scattered in the ipsilateral VA and ECA, which can be explained by stenosis of these arteries, or absent PCoA of CoW or non-active anastomosis through the retrograde ophthalmic artery. FVI in the contralateral VA and ECA was within the age norm.

Cerebral Autoregulation

Figure 2 shows survey results of a patient with symptomatic carotid artery occlusion (transient ischemic attack in the left MCA). Carotid angiography showed the left internal carotid artery occlusion (Figure 2A). The neurological status included intellectual-mnestic and coordinating disorders, elements of sensory aphasia and frontal symptoms, as well as latent right hemiparesis. BP and BFV in both MCA (Figure 2C) were within the normal range. Transcranial Doppler showed a shift of hemodynamic equilibrium from right to left, activation of collateral circulation through the ACoA of the circle of Willis and, to a lesser extent, through the retrograde ophthalmic artery, with a decreased pulsation index in all intracranial arteries. Results of the duplex scanning showed an increase of FVI in the left ECA (Figure 2B). PS between BFV and BP in the M-wave range on the ipsilateral side amounted to 0.2 rad (Figure 2F) with coherence 0.9 (Figure 2E), on the contralateral side – 0.4 rad with coherence 0.9.

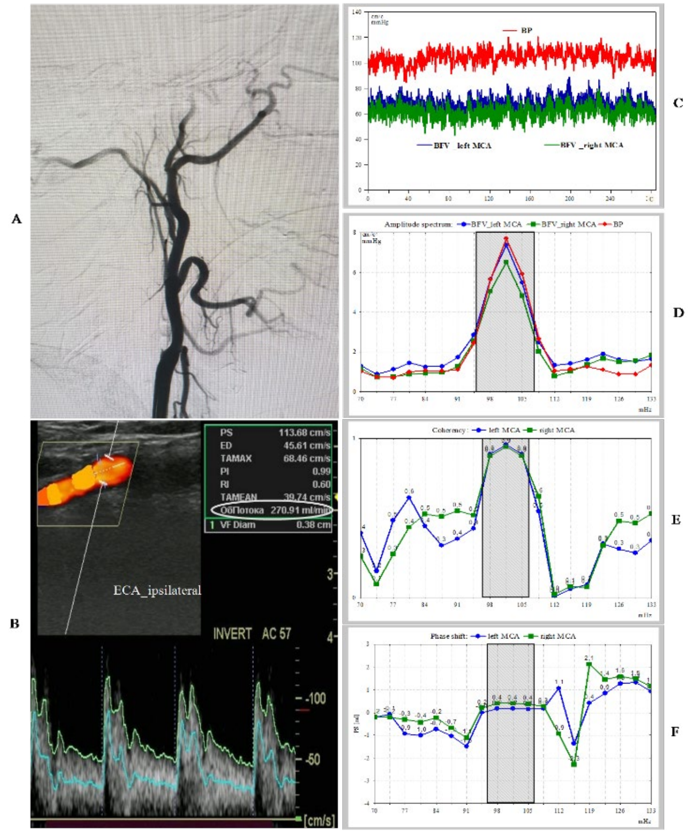

Figure 2: Results of examination of a 60-year-old patient with the left internal carotid artery occlusion: **A**: Left carotid angiogram; **B:** Results of triplex scanning of the ipsilateral External Carotid Artery (ECA); **C:** 5-minute monitoring of systemic Blood Pressure (BP) and Blood Flow Velocity (BFV) in both Middle Cerebral Arteries (MCA); **D:** Amplitude spectrum; **E:** Coherence; **F:** Phase Shift (PS) between spontaneous oscillations of BFV in the MCA and BP in the M-wave range (80-120 mHz).

Figure 3 shows mean values of PS and pulsation index in both MCA in asymptomatic and symptomatic patients. All symptomatic patients had impairment CA on the ipsilateral side: PS was within the range 0.1-0.6 rad. Also, the majority of symptomatic patients had a decreased contralateral PS. BP, BFV and pulsation index in the ipsi- and contrlateral MCA were within the normal range, no significant asymmetry (p> 0.05).

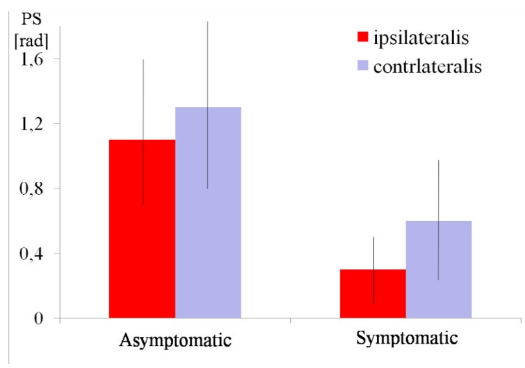

Figure 3: Mean values of the Phase Shift (PS) between spontaneous oscillations in the blood flow velocity in the middle cerebral artery and systemic blood pressure in the Mayer waves in asymptomatic and symptomatic patients with carotid artery occlusion.

Asymptomatic patients had normal CA (Figure 3). Ipsilateral PS ranged within 0.7-1.8 rad, contralateral PS – 0.7–2.2 rad. No significant difference in ipsilateral and contralateral PS ($p > 0.05$) was found. BP and BFV in both MCA were within the normal range.

Discussion

CVR assessment is a key element in determining the treatment tactics for patients with carotid artery occlusion [17]. CVR can be assessed by using both CO_2 reactivity and the state of CA. CA is a basic phenomenon of the cerebral circulation that ensures constant cerebral blood flow when cerebral perfusion pressure changes. Analysis made by R. Grubb et al. [18], shows that in case of a decreased CVR (sub-compensated stage), the risk of stroke is much higher. Therefore, for this group of patients revascularization surgery will be most beneficial [18].

Some researches state that in most symptomatic patients, CVR, measured by the state of CA, is reduced [4,5,19,20]. Our results confirm this statement. All symptomatic patients had impaired CA on the ipsilateral side. Decreased contralateral PS might have occurred due to stenosis of the contralateral ICA in 44% of patients. However, in all patients of this group, collateral blood flow was activated both through the ACoA and PCoA of the CoW and through collaterals of the ECA (9 patients with active anastomosis through the retrograde ophthalmic artery). This was confirmed by an increased BFV and a decreased pulsation index in the contralateral ACA and the ipsilateral PCA, and an increased FVI in the contralateral ICA and the ipsilateral VA and ECA.

Patients with sufficient CA had active collateral blood flow mainly through the ACoA and PCoA of the CoW. This was confirmed by an increased BFV and a decreased pulsation index in the contralateral ACA and the ipsilateral PCA, respectively, and an increased FVI in the contralateral ICA and ipsilateral VA. In should be noted that active anastomosis through the retrograde ophthalmic artery was detected only in 3 cases.

Currently, despite the many studies, there is no unambiguous tactics in Russia or abroad for managing patients with carotid artery occlusion. Relevance of revascularization surgery must rely on a multi-parametric approach with stroke risk assessment. Indications for extra-intracranial bypass surgery in case of carotid artery occlusion should be determined carefully and involve additional criteria. The main criterion is CVR, which can be assessed by both invasive and non-invasive methods. Methods of positron emission tomography are expensive, invasive, and semi-quantitative. Method of CO_2 reactivity assessment is not always possible or safe for this category of patients. Thus, CVR can be best assessed by using the state of CA, intensity of collateral circulation and FVI in the precerebral arteries. These methods are based on analysis of cerebral hemodynamic pathogenesis and can serve well in selecting an individual treatment strategy for patients with carotid artery occlusion. Some researchers believe that assessment of CVR can help to identify symptomatic and asymptomatic patients, who do not need extra-intracranial bypass surgery [17,21]. For instance, in patients with sufficient CVR (unimpaired CA or unchanged CO_2 reactivity), such surgery is considered ineffective and irrelevant [21-23]. Study made by H. Kataoka et al. [21], showed that in case of depleted CVR (de-compensated stage), extra-intracranial bypass surgery will not be effective. The researchers also conclude that in case of a decreased CVR, revascularization surgery is necessary [21]. Apparently, extra-intracranial bypass surgery must be made at a sub-compensated stage of hemodynamic failure, which can be confirmed by a moderately impaired CA.

Confirmed pressure gradient in the donor and recipient vessels is also very important in selecting in favor of revascularization surgery. During the pre-surgery stage, pressure in the donor vessel can be measured by a non-invasive method, indirectly, judging by an increased FVI in the ipsilateral ECA.

Conclusion

A comprehensive approach to the study of cerebral hemodynamics based on assessment of the CA and blood flow redistribution in the precerebral arteries allows an objective identification of hemodynamic failure stage in patients with carotid artery occlusion. Application of noninvasive methods for assessing CVR in medical practice will ensure a differentiated approach to selection of individual treatment tactics for each patient.

Declaration of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Compliance with ethical principles

The authors confirm that they respect the rights of the people participated in the study, including obtaining informed consent.

Funding

This research work was supported by project No. 19-29-01190\19 proposed by Russian Foundation for Basic Research.

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