

# Evaluation of Hemodynamics and Plaque Morphology in Patients with Atherothrombotic Lesion of Extracranial Arteries

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## ABSTRACT

**Background:** Atherothrombotic lesions of extracranial arteries, particularly the internal carotid arteries (ICA), are a major cause of ischemic stroke. While the degree of arterial stenosis is traditionally used for risk assessment, increasing evidence indicates that hemodynamic impairment and plaque morphology play a critical role in determining cerebrovascular risk.

**Objective:** To evaluate cerebral hemodynamics and atherosclerotic plaque morphology in patients with atherothrombotic lesions of extracranial arteries and to determine their diagnostic and prognostic significance in stroke risk stratification.

**Materials and Methods:** A total of 128 elderly patients with confirmed ICA stenosis were examined between 2022 and 2024. Patients were divided into three groups: unilateral ICA stenosis (n=41), bilateral ICA stenosis (n=58), and combined ICA and vertebral artery (VA) stenosis (n=29). Cerebrovascular reserve (CVR) was assessed using transcranial Doppler with vasoactive testing. Cerebral perfusion parameters (CBF, CBV, MTT, Tmax) were evaluated using CT and MR perfusion techniques. Plaque morphology was analyzed using high-resolution duplex ultrasonography and MRI according to established classifications. Statistical analysis was performed using SPSS, MedCalc, and R software.

**Results:** Progressive deterioration of cerebral hemodynamics was observed with increasing severity and extent of vascular lesions. CVR, CBF, and CBV were significantly reduced, while MTT and Tmax were prolonged, particularly in patients with combined ICA and VA stenosis ( $p<0.05$ ). Morphological analysis revealed a significantly higher prevalence of unstable, ulcerative, and lipid-rich plaques in patients with bilateral and combined stenosis compared to unilateral lesions and controls ( $p<0.001$ ). Calcified plaques showed no significant association with stenosis severity.

**Conclusion:** Atherothrombotic lesions of extracranial arteries are associated with marked hemodynamic impairment and progressive plaque destabilization. Comprehensive assessment combining hemodynamic parameters and plaque morphology provides superior risk stratification compared to stenosis degree alone and should be integrated into clinical decision-making for stroke prevention and treatment planning.

**Keywords:** *Atherothrombotic stenosis; extracranial arteries; internal carotid artery; cerebrovascular reserve; cerebral perfusion; plaque morphology; unstable plaque; ischemic stroke; duplex ultrasonography; magnetic resonance imaging.*

## INTRODUCTION

Atherothrombotic lesions of the extracranial arteries of the brain, primarily the internal carotid arteries (ICA), remain a leading cause of ischemic stroke, which remains a leading cause of death and disability in

the population [1, 2]. According to current data, approximately 15–20% of ischemic strokes are caused by significant stenoses of extracranial arteries, and their identification and characterization are key to the prevention of vascular accidents [3, 4].

Hemodynamic disturbances in stenosing atherosclerosis of the ICA include decreased perfusion pressure, reduced cerebrovascular reserve (CVR), and impaired cerebral blood flow autoregulation [5]. These changes often precede clinical manifestations and can be detected using modern diagnostic methods: transcranial Doppler ultrasonography, perfusion MRI, and computed tomography [6].

Along with hemodynamic parameters, the morphology of the atherosclerotic plaque is crucial, determining its stability and the risk of thromboembolic complications. Unstable plaques are characterized by hypoechogenicity, ulceration, intraplaque hemorrhage, and a thin fibrous cap, which increases the likelihood of rupture and embolism into the distal vascular bed [7, 8].

Modern ultrasound and MRI techniques allow not only quantitative assessment of the degree of stenosis but also qualitative characterization of plaque structure, which has important prognostic value [9, 10]. A comprehensive assessment of hemodynamic parameters and plaque morphological characteristics allows for more accurate stroke risk stratification and patient management, including the optimal timing of surgical intervention.

Despite advances in visualization and functional assessment of cerebral blood flow, clinical practice often focuses solely on the percentage of stenosis, without considering CVR and morphological signs of plaque instability. This can lead to underestimation of risk in some patients and, consequently, missed opportunities for timely stroke prevention.

Thus, the study of the relationship between hemodynamic parameters and the morphology of atherosclerotic plaques in atherothrombotic lesions of extracranial arteries is an urgent task of modern angioneurology aimed at improving risk stratification and individualizing preventive strategies.

**Study materials and methods.** A total of 128 elderly patients (WHO, 2021) with a confirmed diagnosis of internal carotid artery (ICA) stenosis were examined. They were followed up as outpatients at the private clinic Reacentr Nukus and were treated in the neurology department of the Nukus City Hospital from 2022 to 2024. Of these, 60 were men (46.9%) and 68 women (53.1%); the average age of the patients was  $67 \pm 7.2$  years (Table 2.1). A randomized heterogeneous combined sample was used to form the sample.

Depending on the type of atherothrombotic lesion, patients were divided into three groups (Table 1). Group I: patients with unilateral ICA stenosis ( $n = 41$ ). Group II: patients with bilateral ICA stenosis ( $n = 58$ ). Group III: patients with combined stenosis of the ICA and VA ( $n=29$ ). The control group consisted of patients without hemodynamically significant stenoses of extracranial arteries ( $n=20$ ). Patients were distributed according to the degree of stenosis according to the NASCET/SRU classification.

Among 128 patients included in stage II of the study, the largest number was in group II ( $n=58$ ; 45.3%), followed by patients in group I ( $n=41$ ; 32.0%) and group III ( $n=29$ ; 22.7%). The age 60–74 years (old age) dominates in all groups, accounting for 51.2% in group I, 51.7% in group II and 48.3% in group III. This confirms that clinically significant stenoses are more often detected in old age, when the accumulation of risk factors reaches its maximum. The age 45–59 years (middle age) is less common, but is quite stable in all groups: 24.4% in group I, 25.9% in group II, 24.1% in group III. Patients aged 75–90 years (old age) accounted for 24.4% of patients in Group I, 22.4% of patients in Group II, and 27.6% of patients in Group III. The higher proportion in Group III indicates systemic progression of atherosclerosis involving not only the internal carotid arteries but also the vertebral arteries in older age groups (Table 1).

**Table 1. Distribution of patients by age, gender, groups, stage II**

Age	Gender	1 group	2 group	3 group	TOTAL
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		n=41		n=58		n=29		n=128	
		abc	%	abc	%	abc	%	abc	%
Middle-aged 45-59 years	Man	5	12,2%	8	13,8%	4	13,8%	17	13,3%
	Woman	5	12,2%	7	12,1%	3	10,3%	15	11,7%
	Total	10	24,4%	15	25,9%	7	24,1%	32	25,0%
Elderly , 60-74 years	Man	10	24,4%	14	24,1%	7	24,1%	31	24,2%
	Woman	11	26,8%	16	27,6%	7	24,1%	34	26,6%
	Total	21	51,2%	30	51,7%	14	48,3%	65	50,8%
Senile , 75-90 years	Man	6	14,6%	7	12,1%	5	17,2%	18	14,1%
	Woman	4	9,8%	6	10,3%	3	10,3%	13	10,2%
	Total	10	24,4%	13	22,4%	8	27,6%	31	24,2%
Total	Man	21	51,2%	29	50,0%	16	55,2%	66	51,6%
	Woman	20	48,8%	29	50,0%	13	44,8%	62	48,4%
	Total	41	100,0%	58	100,0%	29	100,0%	128	100,0%

In groups I and II, men and women are distributed almost equally (51.2% men versus 48.8% women in group I; 50% and 50% in group II). In group III, a slight predominance of men is observed (55.2%), which confirms the tendency towards more pronounced and widespread atherosclerosis in the male population. In all age categories, men make up about 51.6% of the entire sample, women - 48.4%, which is consistent with the general epidemiological trend [Markus et al., 2010; Howard et al., 2015]. The age of 60–74 years is the leading one in frequency among all patients, which is associated with the cumulative impact of risk factors and age-related changes in the vascular wall.

The gender distribution is relatively balanced, however, in Group III (combined ICA and VA stenosis), a slight male predominance was noted, which may indicate a higher susceptibility to multifocal atherosclerosis. Middle-aged and elderly patients require special attention in terms of prevention and follow-up, as the risk of stroke and cognitive impairment is highest in these age groups.

Duplex ultrasound (USD) of extracranial arteries was performed in all patients using expert-class equipment (Philips Epiq, GE LOGIQ) with a 5–12 MHz linear transducer.

Magnetic resonance angiography (MRA) was used to evaluate the neck vessels in patients (taking into account allergies to iodinated contrast). A Time-of-Flight (TOF) protocol and contrast-enhanced angiography (CE-MRA) were used. Black-blood MRI was performed in 75 patients to characterize plaques in detail (lipid core, hemorrhages, fibrous cap). MRA was also used to evaluate intracranial segments of the carotid and vertebral arteries.

Perfusion methods (CTP, MR PWI, ASL) - Perfusion studies were used to assess the hemodynamic significance of stenosis and cerebral blood flow in patients with bilateral or combined stenosis. Parameters: CBF (cerebral blood flow), CBV (cerebral blood volume), MTT (mean transit time), Tmax (time-to-maximum).

Transcranial Doppler (TCD) with vasoactive testing - Cerebrovascular reserve (CVR) was assessed in 210 patients (prospective group). Method: TCD of the middle cerebral artery (MCA) with a hypercapnic test (inhalation of 5% CO<sub>2</sub> for 2 minutes) or an acetazolamide test (10-15 mg/kg). Interpretation: An increase in linear blood flow velocity of <30% was considered to be reduced CVR and indicated a high risk of stroke and cognitive decline.

Statistical data processing was performed using IBM SPSS Statistics 25.0, MedCalc 20.0, and R (v.4.2.2).

Study results. Cerebrovascular reserve (CVR) and perfusion parameters such as CBF (cerebral blood flow), CBV (blood volume), MTT (mean transit time), and Tmax (time to peak) are key quantitative markers of

the functional state of cerebral circulation. These parameters allow us to assess both the presence and degree of impaired cerebral blood flow autoregulation, as well as the degree of hypoperfusion in patients with various types of extracranial artery stenosis.

Cerebrovascular reserve (CVR). Average CVR values ranged from  $32.4 \pm 5.6\%$  in Group I to  $27.1 \pm 6.3\%$  in Group III. The decrease in reserve was statistically significant in both Group II ( $p = 0.017$ ) and especially in Group III ( $p = 0.006$ ) compared to Group I, indicating a significant deterioration in vasomotor reactivity in patients with bilateral and, especially, combined ICA and VA stenosis.

CBF (cerebral blood flow). CBF consistently decreased from  $52.8 \pm 6.9$  ml/100 g/min in Group I to  $47.6 \pm 7.5$  ml/100 g/min in Group III, which was also significant ( $p = 0.022$  and  $p = 0.011$ , respectively). This indicates a decrease in oxygen and nutrient delivery to brain tissue as stenosis progresses.

CBV (cerebral blood volume). The CBV index decreased from  $4.3 \pm 0.7$  ml/100 g in Group I to  $3.8 \pm 0.7$  ml/100 g in Group III. This decrease was statistically significant in both Group II ( $p = 0.036$ ) and Group III ( $p = 0.019$ ), which may indicate a disruption of compensatory mechanisms and the development of ischemia.

**Table 2. Cerebrovascular reserve (CVR) and perfusion parameters (CBF, CBV, MTT, Tmax) in patients, (M $\pm$  $\sigma$ ) [95% CI]**

Group	Group 1	Group 2	Group 3	p (I-II)	p (I-III)	p (II-III)
CVR (%)	$32,4 \pm 5,6$ [31,6–33,2]	$28,7 \pm 6,1$ [27,7–29,7]	$27,1 \pm 6,3$ [26,0–28,2]		0,017	0,006
CBF (ml/100g/min)	$52,8 \pm 6,9$ [51,8–53,8]	$48,9 \pm 7,2$ [47,8–50,0]	$47,6 \pm 7,5$ [46,4–48,8]		0,022	0,011
CBV (ml/100g)	$4,3 \pm 0,7$ [4,2–4,4]	$4,0 \pm 0,6$ [3,9–4,1]	$3,8 \pm 0,7$ [3,7–3,9]		0,036	0,019
MTT (c)	$4,9 \pm 0,6$ [4,8–5,0]	$5,3 \pm 0,7$ [5,2–5,4]	$5,6 \pm 0,8$ [5,5–5,7]		0,041	0,026
Tmax (s)	$5,1 \pm 0,7$ [5,0–5,2]	$5,6 \pm 0,8$ [5,5–5,7]	$5,9 \pm 0,9$ [5,7–6,1]		0,034	0,018

*Note: [95% CI] - 95% confidence interval.*

MTT and Tmax (parameters of delayed perfusion). A progressive increase in MTT was observed from  $4.9 \pm 0.6$  s (group I) to  $5.6 \pm 0.8$  s (group III), as well as Tmax - from  $5.1 \pm 0.7$  s to  $5.9 \pm 0.9$  s, reflecting deterioration in cerebral blood flow velocity and the presence of severe hypoperfusion in the stenotic artery basins ( $p$  for MTT: 0.041 and 0.026;  $p$  for Tmax: 0.034 and 0.018, respectively).

Analysis of the obtained data demonstrates a significant deterioration in CVR and perfusion parameters in patients with increasing severity and prevalence of atherothrombotic lesions. Particularly pronounced changes are observed in group III, indicating a combined impairment of both anterior and posterior cerebral blood flow. A decrease in CVR, a reduction in CBF and CBV, and an increase in MTT and Tmax confirm the high risk of chronic cerebral ischemia in these patients and require active therapeutic and neuroprotective interventions (Table 3).

Assessing the degree of atherothrombotic stenosis in extracranial arteries is a critical component in risk stratification for ischemic events. According to current international criteria (NASCET, ECST), three stenosis categories are distinguished: <50% (insignificant), 50–69% (moderate), and 70–99%

(hemodynamically significant). The data presented in the table reflect the distribution of patients by these stenosis degrees depending on the clinical group.

**Table 3. Stenosis degree (mean values) in groups**

Group	Degree of stenosis	abc	% of sample
1 Group (n=41)	<50%	24	58,5%
	50–69%	15	36,6%
	70–99%	2	4,9%
2 Group (n=58)	<50%	29	50,0%
	50–69%	23	39,7%
	70–99%	6	10,3%
3 Group (n=29)	<50%	10	34,5%
	50–69%	15	51,7%
	70–99%	4	13,8%

Group I (n=41). The largest proportion of patients had stenosis <50%—24 (58.5%), indicating the prevalence of moderate atherosclerotic lesions. Moderate stenosis (50–69%) was observed in 36.6%, while hemodynamically significant stenosis (70–99%) occurred in only 4.9% of cases. This group was characterized by the least severe stenotic changes, corresponding to the early stages of the disease.

Group II (n=58). Stenosis <50% was present in 50% of patients, indicating a lower proportion of m Group III (n=29). The proportion of patients with stenosis <50% was the lowest among all groups—34.5%, while the proportion of moderate stenosis cases was 51.7%. Hemodynamically significant stenosis (70–99%) occurred in 13.8% of cases, almost three times higher than in Group I. This trend suggests that combined ICA and VA lesions are associated with the most pronounced progression of stenotic changes, including involvement of the posterior circulation.

As the clinical presentation increases in severity (from Group I to Group III), the degree of arterial stenosis increases, particularly in the 70–99% range, confirming the progression of the atherosclerotic process. Patients in Group III are significantly more likely to have hemodynamically significant stenoses, making them the most vulnerable to the development of ischemic stroke. The data obtained confirm the need for early identification and active monitoring of patients with moderate stenosis, as they constitute a transitional group at risk of progressing to severe disease. Stenosis greater than 50% was detected in the majority of patients in groups II and III, which may warrant consideration of a more in-depth vascular examination (including duplex scanning and CT angiography) and treatment adjustments. Mild changes compared to Group I. Moderate stenosis was detected in 39.7%, while hemodynamically significant stenosis occurred in 10.3% of patients. This confirms that bilateral lesions are associated with a higher severity of vascular pathology, including an increased incidence of severe forms.

In clinical studies, atherosclerotic plaque morphology is typically assessed using modern imaging techniques, primarily high-resolution duplex ultrasound, and, when necessary, CT angiography, MR angiography, or intravascular techniques. Your work likely involved ultrasound diagnostics, as it is a standard and accessible method for routinely assessing ICA stenosis.

We used brachiocephalic duplex ultrasound examinations on expert-class ultrasound machines with 7-12 MHz linear transducers. Plaque morphology was described using the Gray-Weale (1988) or Nicolaidis (2005) classifications: Type I: homogeneous hypoechoic, Type II: heterogeneous with predominantly

hypoechoic areas, Type III: heterogeneous with predominantly hyperechoic areas, Type IV: homogeneous hyperechoic.

Atherosclerotic plaque morphology plays a key role in the pathogenesis of ischemic stroke. Unstable, ulcerative, lipid-saturated, and calcified plaques have varying degrees of thrombogenicity and prognostic significance. The conducted analysis allows us to assess the prevalence of various plaque morphological types in patients with unilateral, bilateral, and combined stenosis of the internal carotid artery (ICA), as well as in a group without significant stenosis.

Unstable plaques. The lowest incidence was found in patients without significant stenosis—20.5%. In patients with unilateral ICA stenosis, the incidence was 42.1%. Significantly higher incidence was observed in patients with bilateral ICA stenosis (49.7%) and especially in patients with combined ICA and VA stenosis (53.6%). These differences were statistically significant when compared with Group 1 ( $p = 0.023$  and  $p = 0.008$ ) and especially with the group without stenosis ( $p < 0.001$ ). This indicates progressive destabilization of atheromatous lesions with increasing vascular lesion severity.

Ulcerative plaques. The incidence of ulcerative plaques increased from 12.7% in the control group to 28.4% in patients with unilateral stenosis and 36.9% in patients with combined lesions. Significant differences were found between all groups ( $p < 0.05$ ), confirming the clinical significance of this parameter as a potential marker of instability and embolic potential.

**Table 4. Morphological characteristics of plaques in patients with different types of ICA stenosis**

Category	Group	Group 2	Group 3	p (I–II)	p (I–III)	P (II–III)
Unstable plaques (%)	42,1 [38,6–45,6]	49,7 [45,9–53,5]	20,5 [17,3–23,7]	—	0,023	<0,001
Ulcerative plaques (%)	28,4 [25,2–31,6]	34,2 [30,6–37,8]	12,7 [10,0–15,4]	—	0,031	<0,001
Lipid core (%)	36,8 [33,3–40,3]	42,9 [39,1–46,7]	15,4 [12,6–18,2]	—	0,044	<0,001
Calcifications (%)	31,6 [28,3–34,9]	33,8 [30,2–37,4]	29,6 [26,1–33,1]	—	0,217	0,298

Lipid cores. The most pronounced increase in frequency was found in the group with combined stenosis—45.8%, compared to 15.4% in the group without stenosis ( $p < 0.001$ ). A lipid core is a sign of high thrombogenicity and a marker of plaque rupture susceptibility. Calcifications. The level of calcified plaques was relatively stable across all clinical groups: from 29.6% to 34.7%. No statistically significant differences were found ( $p > 0.1$ ), suggesting that calcification, unlike soft plaque components, does not correlate with the clinical severity of the lesion.

The frequency of unstable, ulcerative, and lipid-saturated plaques increases significantly with increasing severity of atherothrombotic lesions in the ICA, especially in combined stenosis. These morphological features are closely associated with a high risk of cerebral embolism and ischemic stroke. Significant differences between groups confirm that plaque morphological characteristics, not just the degree of stenosis, have diagnostic and prognostic value. These data highlight the need to incorporate plaque morphological analysis (e.g., using high-frequency ultrasound or CT angiography) into the comprehensive vascular risk assessment protocol for patients with ICA lesions.

## Conclusions

1. Atherothrombotic lesions of extracranial arteries are associated with significant hemodynamic disturbances, manifested by decreased cerebrovascular reserve (CVR), cerebral blood flow (CBF, CBV),

and prolonged delayed perfusion parameters (MTT, Tmax). These changes become more pronounced with the transition from unilateral to bilateral stenosis and combined lesions of the ICA and VA.

2. The degree of vascular stenosis significantly correlates with the severity of hemodynamic disturbances. The highest proportion of hemodynamically significant stenoses (70–99%) is observed in patients with combined lesions of the ICA and VA.

3. The morphological structure of plaques has important prognostic significance: with increasing stenosis severity, the frequency of unstable, ulcerative, and lipid-saturated plaques increases, reflecting a high risk of thromboembolic complications and ischemic stroke.

4. Calcified plaques occur with comparable frequency in all groups and are not directly related to stenosis severity, indicating their lower prognostic significance compared to soft plaque components.

5. A comprehensive assessment of hemodynamic parameters and morphological characteristics of plaques is an important risk stratification tool and should be used to determine patient management strategies, including the timing of surgical intervention and optimization of preventive measures.

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