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The importance of blood flow volume in the brain-supplying arteries for the clinical management – the impact of collateral circulation

Michał Elwertowski¹, Jerzy Leszczyński¹, Piotr Kaszczewski¹,
Krzysztof Lamparski², Stella Sin Yee Ho³, Zbigniew Gałązka¹

¹ Department of General and Endocrinological Surgery, Medical University of Warsaw, Warsaw, Poland

² Department of Radiology, Medical University of Warsaw, Warsaw, Poland

³ Department of Imaging and Interventional Radiology, The Chinese University of Hong Kong, Shatin, SRA Hongkong, China

Correspondence: Michał Elwertowski, Department of General and Endocrinological Surgery, Medical University of Warsaw, Banacha 1A, 02-097 Warsaw, Poland
e-mail: elwertowski.michal@gmail.com

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Abstract

Aim: An assessment of increased compensatory blood flow in the brain-supplying arteries in patients with significant carotid artery stenosis. **Materials and methods:** Doppler ultrasound was performed in 218 patients over 60 years of age to evaluate both the degree of brain-supplying artery stenosis as well as the blood flow volume balance in all vessels supplying the brain: the internal carotid artery, the external carotid artery and the vertebral artery. The control group included 94 patients with no stenosis in the extracranial segments and no neurological manifestations, in whom blood flow values were calculated (the internal carotid artery – 290 mL/min, the external carotid artery – 125 mL/min, the vertebral artery – 80 mL/min); the total mean blood flow in the brain-supplying arteries was 985 mL/min. A 33% increase in blood flow was considered compensatory. In addition to the control group, 30 patients with asymptomatic stenosis of less than 50% and 12 patients after endarterectomy with mean blood flow of 920 mL/min and 960 mL/min, as well as two groups of particular interest to us, i.e. 38 patients with no compensatory blood flow increase despite significant stenosis (>50%) with mean blood flow of 844 mL/min and 44 patients with similar stenosis and with compensatory blood flow increase up to 1174 mL/min were included in the analysis. **Results:** Comparison of the two groups showed several significant differences: increased blood flow (118% vs. 86% of the norm) in patients with compensated stenosis, an increased number of asymptomatic patients (70% vs. 37%) and a threefold increase in the number of patients with occlusions (15 : 5) in the group of patients with increased blood supply to the brain. **Conclusions:** All potential blood-supplying vessels, including the external carotid artery, are involved in brain tissue perfusion in some of the patients with significant stenosis. Determining the degree of compensation may have an important impact on the indications for surgical treatment, which will make a valuable contribution to the current criteria (asymptomatic/symptomatic patients).

Introduction

Stenosis of the brain-supplying arteries is a serious clinical problem faced by both neurologists providing healthcare services to patients, as well as vascular surgeons and interventional radiologists involved in treatment processes. Ischemic stroke accounts for about 80% of all neurological incidents, 30% of which are due to brain-supplying arterial stenosis involving segments that can be subjected to surgical repair^(1,2). The past 27 years (since the publication of the preliminary NASCET results in 1991) have seen changes in the approach to patient management, surgical procedure qualification and stent placement. A departure from a purely mechanical qualification for surgical intervention of all stenoses of more than 70% and the introduction of different indications for men (70%) and women (80%) may be observed in the field of imaging diagnostics⁽³⁾. Other factors influencing patient management, particularly plaque echogenicity: regular/irregular surface, the presence and the shape of plaque defects, as well as patient's age and clinical condition, started to be taken into account. Parameters for unstable atherosclerotic plaque were determined, such as a hypoechoic plaque or a plaque with a small echogenic component, with irregular surface containing defects, a lipid core and thrombi. The risk associated with different elements of the ultrasonographic image and hemodynamic disorders related to vascular stenosis is known. Physiological processes that occur in the carotid vessels of patients with atherosclerotic lesions as well as those occurring in the atherosclerotic plaque have been described⁽⁴⁾. It is currently possible to monitor changes occurring in the vessels as a result of pharmacotherapy (statins). A clinical division into symptomatic and asymptomatic patients with significant vascular stenosis was introduced with the consolidation of diversified therapeutic management, limiting the indications for surgical treatment in patients with no clinical symptoms.

Ultrasonography is the most common imaging technique used for the evaluation of carotid and vertebral arteries. Due to its non-invasive nature, availability and low cost as well as the absence of risks associated with radiographic imaging, ultrasonography has become the basic tool for the assessment of vascular stenosis. Ultrasound limitations include low repeatability and interpretation discrepancies in the assessment of images by different doctors who perform the scanning⁽⁵⁾. CT-angiography is the method of choice in the case of doubts, technical difficulties faced during vascular scanning or problems with obtaining a Doppler signal due to long, calcified plaques or anatomical obstacles.

The paper presents a different method for the assessment of the effects of carotid stenosis on cerebral circulatory hemodynamics, which allows for a global evaluation of blood supply to the brain and the interactions between blood vessels due to the presence of their physiological connections and the degree of collateral circulation in cases of impaired blood flow in one (or more) of these vessels.

Materials and methods

A group of 218 patients over 60 years of age were included in the analysis. A detailed blood flow evaluation of the brain-supplying arteries, including a morphological assessment of atherosclerotic lesions, Doppler measurements of changes in the blood flow velocity in terms of the degree of vascular stenosis, as well as flow volumetry to determine the involvement of different arteries in cerebral circulation, was performed. Under physiological conditions, the cerebral blood flow is about 750–850 mL/min, accounting for about 14% of ejection fraction. It should be noted, however, that cerebral perfusion declines with age in a manner that is sometimes difficult to predict⁽⁶⁾.

The patients were referred for Doppler ultrasonography due to neurological findings suggesting stenosis of the extracranial vessels as one of the potential causes for their symptoms. The control group included patients with no significant symptoms suggesting cerebral circulatory pathology, who were age-matched to the study group.

Two ultrasound scanners were used in the study: Aloka F75 and Toshiba Aplio 500, both with vascular transducers and semiautomatic programs, allowing for flow volumetry.

The site of Doppler measurement is of key importance. The internal carotid arteries (ICAs) were measured in their upper segments 3–4 cm above the ICA bulb to avoid false results due to changes in velocity around the atherosclerotic plaques, which are usually present in the proximal vascular sections, in straight segment, where physiological, parabolic velocity profile of flow was observed. The external carotid arteries were evaluated in their middle segments, above the origin of the upper thyroid artery to avoid false results due to thyroid pathologies. Vertebral arteries were evaluated in their possibly straight segments with signal registration at V2 (V1 in the case of a tortuous course and technical difficulties). Vascular diameter measurements using good quality color images were performed directly on the screen with flow velocity recording. High settings for color recording rate, i.e. above 30–40 cm/second, were used to avoid false results. In the case of doubts, arterial diameter was measured prior to velocity recording, and the obtained values were used to calculate the volume from triplex image, with the recording of mean blood flow velocity in the assessed vessels. This type of situation was particularly frequent during flow volumetry in narrower vertebral arteries with minimal blood flow, which did not allow obtaining a reliable color-coded image.

Patients with successfully performed flow volumetry in all main vessels potentially supplying the brain, i.e. internal carotid arteries, vertebral arteries and external carotid arteries, were included in further analysis⁽⁷⁾. Patient classification into groups is shown in Tab. 1.

	No.	Mean age
Controls group	94	63.9
Asymptomatic patients – stenosis up to 40%	30	69.5
Patients after endarterectomy	12	68.5
Stenosis without blood flow compensation	38	70.7
Stenosis with blood flow compensation	44	66.1

Tab. 1. Patient classification

Normal blood flow values for brain-supplying vessels in patients over the age of 60 years were determined based on the examination performed in the control group ($n = 94$). The mean blood flow values were as follows: ICA – 290 mL/min, ECA – 125 mL/min, VA – 80 mL/min. More than a 33% increase in the cerebral blood flow volume in relation to the above standard or a 25% increase with simultaneously elevated volumetry in more than one vessel were considered compensatory.

Results

The obtained results are shown in Tab. 2. The control group included 94 patients with no significant clinical manifestations (referred for scanning due to hypertension, headache and dizziness, malaise, coronary heart disease, aortic and lower limb artery pathology) and with no atherosclerotic lesions causing stenosis revealed by Doppler ultrasound, with mean ICA, ECA and VA blood flow of 985 mL/min. In another group (30 patients), the presence of moderate plaques causing minor stenosis – up to 40%, with an increase in PSV >100 cm/s in 12 cases, EDV >25 cm/s in 17 cases and turbulences in 23 cases was demonstrated. None of the patients had EDV of more than 40 cm/s.

Two groups were of particular interest to us, i.e. patients with significant internal carotid stenosis, but no com-

pensatory blood flow increase in other vessels as well as patients who developed collateral circulation ensuring brain perfusion. Both groups had a similar mean maximum percentage of stenosis, i.e. 67% in the non-compensatory group and 73.3% in patients with increased intracerebral flow. In the non-compensatory group (38), significant ICA stenoses >50% were detected in 23 patients on the right side (2 occlusions) and 15 patients on the left side (3 occlusions), while 6 patients developed bilateral stenosis. In cases of compensatory, increased blood flow (44), the stenotic location was similar: 25 right-sided ICA stenotic lesions and 19 left-sided lesions. Vascular obstruction was diagnosed 3 times more often (15) (right-sided in 9 and left-sided in 6 patients), whereas bilateral stenoses of more than 50% were found in 9 patients. A marked increase in the volume of blood supplied to the brain, exceeding the norm by more than 20%, was found in 35 of 44 patients. The mean volume of blood supplied to the brain in patients with no compensation was 844 mL/min, i.e. 86% of the norm determined based on the measurements performed in the control group, while the same volume was 1174 mL/min (119% of the norm) in patients who developed collateral circulation.

Increased blood flow in a single group of vessels was present in 19 patients: ICA – 9, VA/2VA – 6, ECA/2ECA – 4. Increased blood flow in more than one vessel, involving the remaining inflow vessels (involving ICA, 2ECA and 2VA in 4 patients) was more common (25/44). In total, increased ICA blood flow was found in 23, ECA in 24, and VA in 21 patients; however quantitatively effective increase was most evident in the internal carotid arteries.

Of 14 cases of ICA obstruction, 3 patients had no increased blood flow in the opposite ICA (additionally, bilateral ICA obstructions were found in one patient), and

Przepływ	Blood flow $n = 94$	Asymptomatic $n = 30$	Post-surgical EA $n = 12$	Stenosis with no compensation $n = 38$	Stenosis with compensation $n = 44$
R ICA mL/min	285	234	319	222	239
R ECA mL/min	127	132	97	115	179
R VA mL/min	71	68	83	98	137
L ICA mL/min	295	270	231	208	333
L ECA mL/min	122	126	134	115	156
L VA mL/min	92	98	107	95	141
R ICA velocity cm/s	73/24	103/28	115/35	159/42	126/42
L ICA velocity cm/s	70/24	84/24	162/44	132/37	144/44
R ICA stenosis %	0	28	18	51	55
L ICA stenosis %	0	22	44	48	45
Total blood flow mL/min	985	920	960	844	1174

EEA – endarterectomy; R – right; L – left

Tab. 2. Blood flow volume, mean velocity, mean percentage stenosis and total blood flow in the brain-supplying arteries in different groups of patients

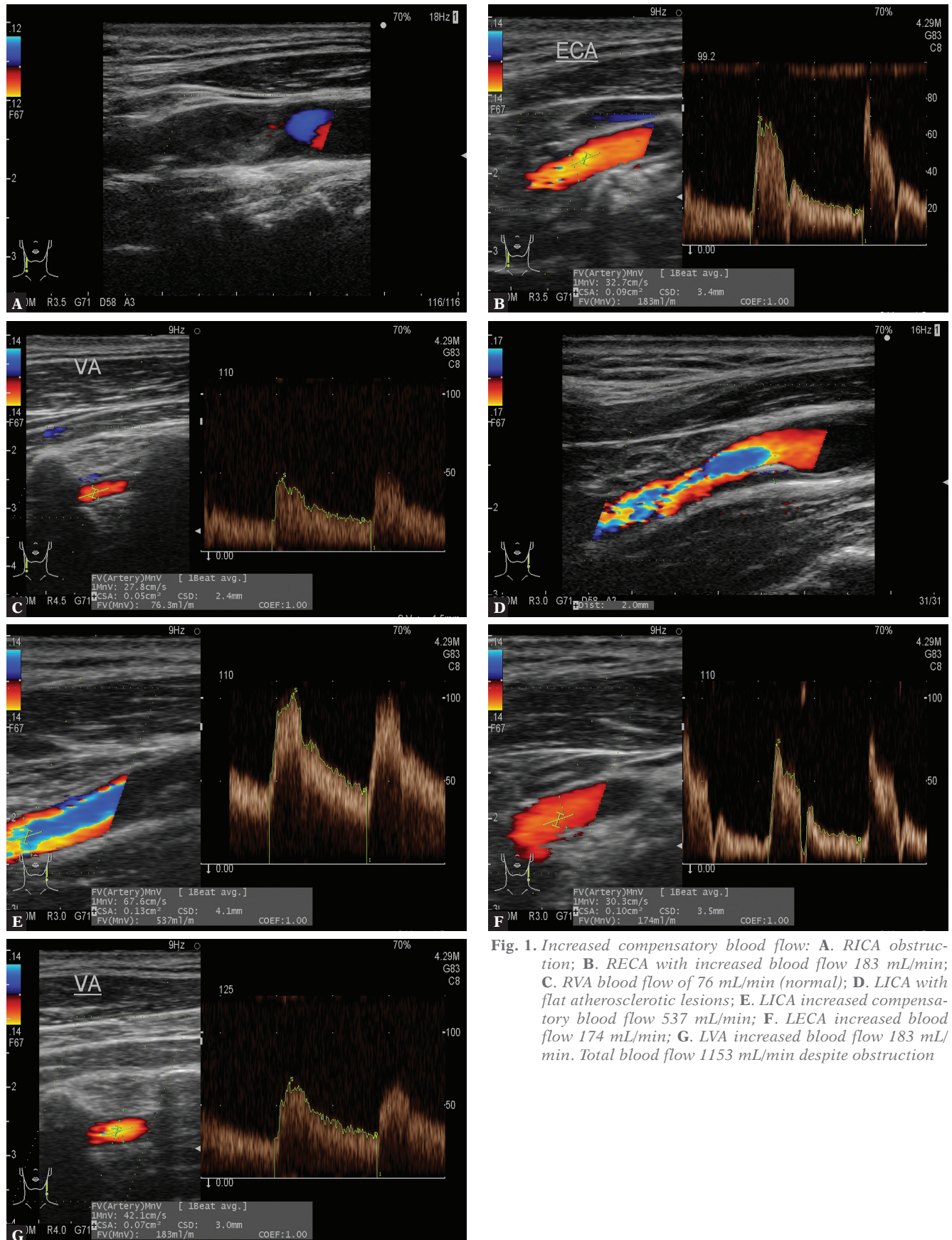


Fig. 1. Increased compensatory blood flow: **A.** RICA obstruction; **B.** RECA with increased blood flow 183 mL/min; **C.** RVA blood flow of 76 mL/min (normal); **D.** LICA with flat atherosclerotic lesions; **E.** LICA increased compensatory blood flow 537 mL/min; **F.** LECA increased blood flow 174 mL/min; **G.** LVA increased blood flow 183 mL/min. Total blood flow 1153 mL/min despite obstruction

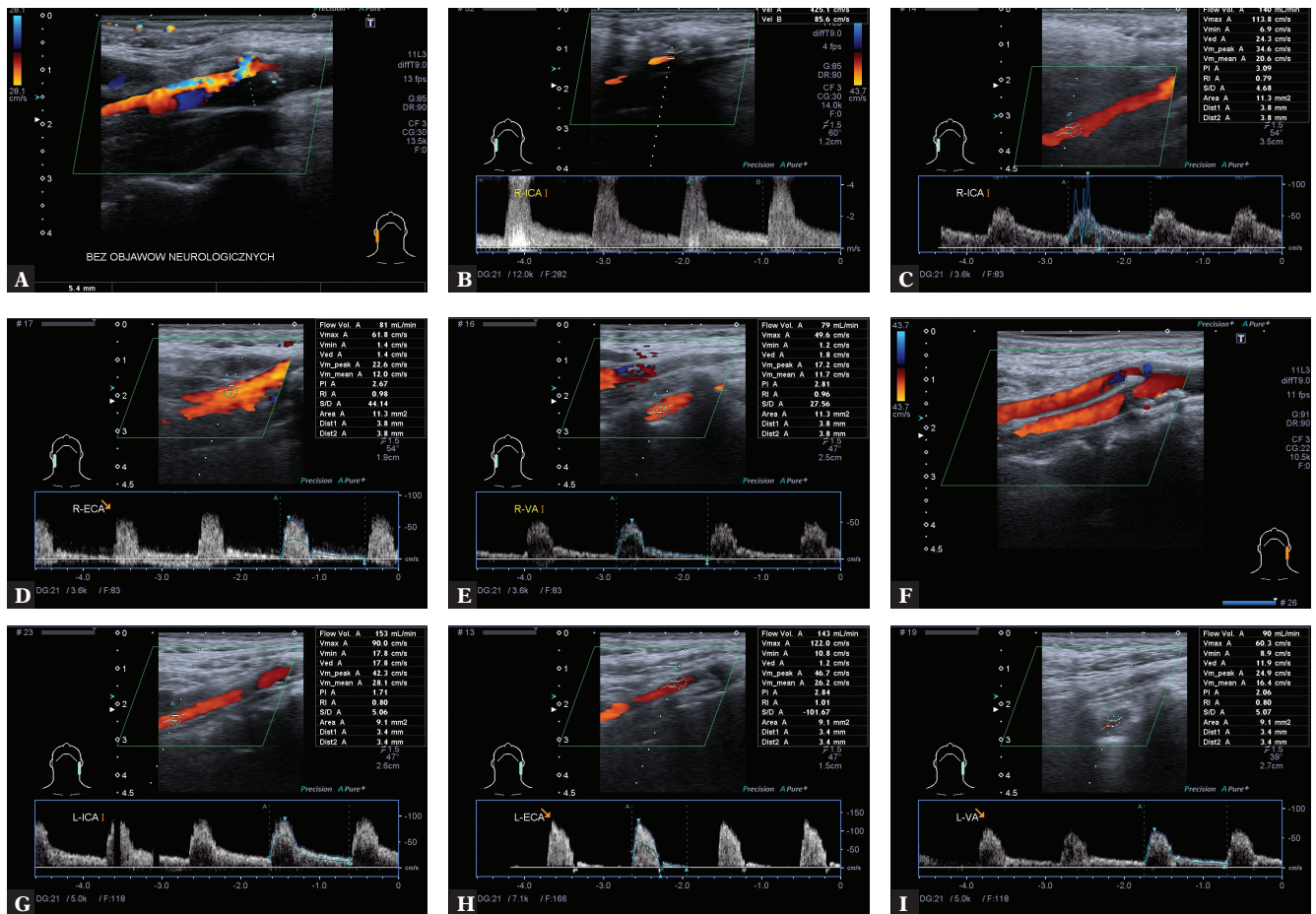


Fig. 2. Uncompensated, asymptomatic RICA stenosis: **A.** Morphology; **B.** Spectral recording of PSV 425 cm/s, EDV 85 cm/s; **C.** Reduced RICA blood flow 140 mL/min; **D.** RECA blood flow 81 mL/min (normal); **E.** RVA blood flow 79 mL/min (normal); **F.** L ICA with flat atherosclerotic lesions; **G.** Decreased LICA blood flow 153 mL/min; **H.** LECA blood flow 143 mL/min (upper limit of normal); **I.** LVA blood flow 90 mL/min (normal). Significantly decreased total blood flow 686 mL/min, the patient is a candidate for interventional treatment

the opposite ICA was the only vessel with increased blood flow in one case. In other patients, increased blood flow was found in most unobstructed vessels (in all five of them in one case). In four cases of ICA-occlusion-related stroke, follow-up ultrasound showed a gradual increase in blood flow in other vessels.

Discussion

Ultrasonographic assessment of the degree of stenosis in the brain-supplying vessels changes with the technical development of equipment and knowledge on the pathophysiological changes in the narrowing brain-supplying vessels. A departure from an unreflective approach to patients with significant stenoses is an additional factor influencing the treatment method. The clinical division into symptomatic and asymptomatic patients, with the predominance of indications for conservative therapy in the latter group, is also more common.

Morphological assessment of the degree of stenosis based on a B-mode image is often unreliable (except for

minor and critical stenosis producing unambiguous images) due to the mechanism of dilation of carotid arteries with developing atherosclerotic lesions⁽¹⁾. This sometimes causes a 30% increase in vascular diameter, and prominent plaques up to a few millimeters thick, which are present in the wall, may not cause significant lumen stenosis requiring intervention. Due to the inter-patient variation in terms of defensive mechanisms, this is an additional factor preventing an assessment of stenotic degree based on the comparison between patent vessel diameter and the total width of the vessel (and even more so surface area measurements). On the other hand, comparing the diameter of a patent vessel at the site of stenosis with the segment located above may produce an error of underestimation in the case of significant stenosis of more than 70–80%^(2,8). In such cases, a decrease in the flow volume (in accordance with the Spencer's Curve) occurs, leading to decreased blood pressure and, consequently, reduced vascular diameter.

Doppler assessment of stenotic degree based on changes in the flow velocity at the sites of the most significant lesions was also subject to evolutionary changes with

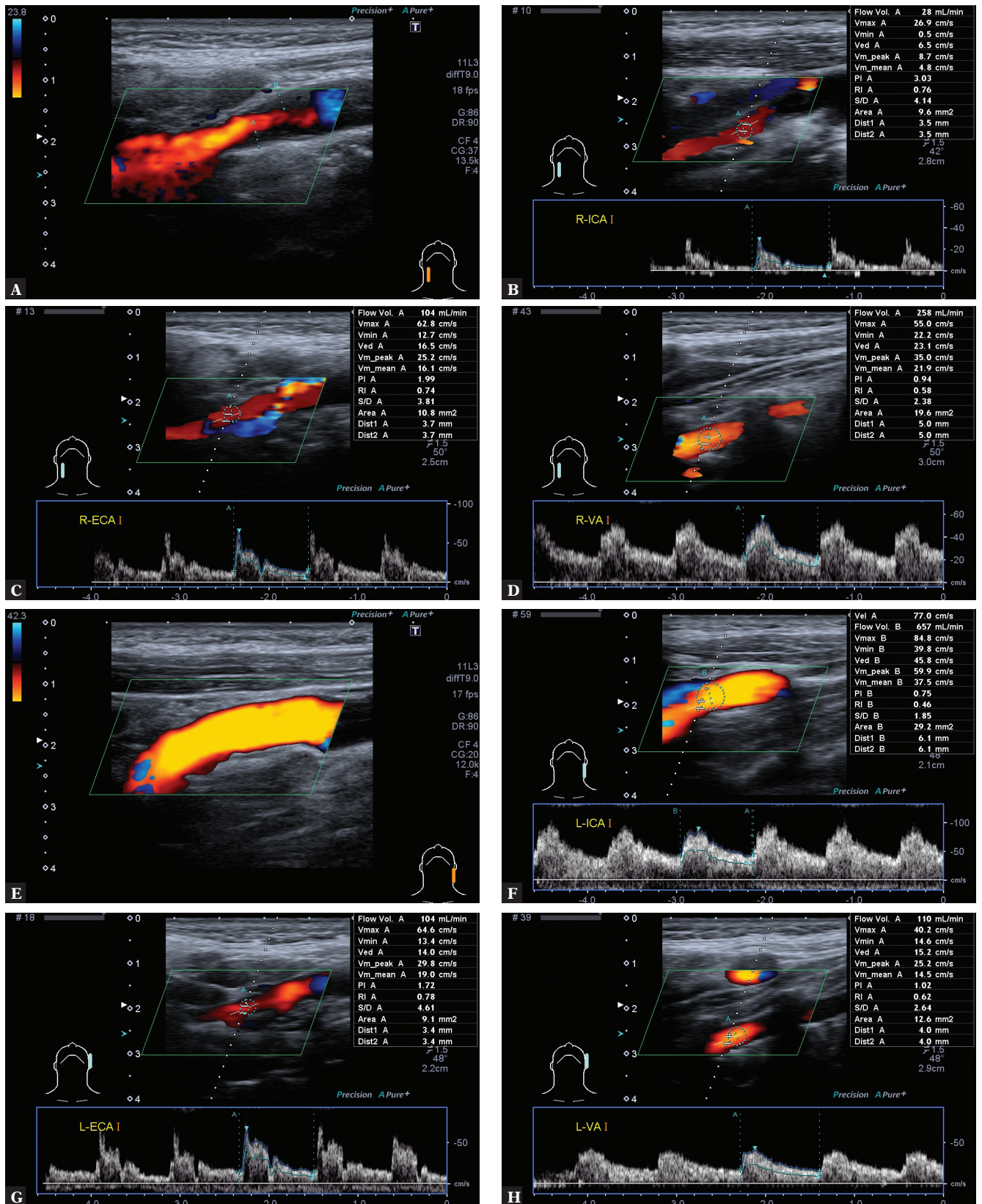


Fig. 3. Compensated, asymptomatic RICA stenosis: **A.** stenosis morphology, about 90–95%; **B.** Decreased RICA blood flow 28 mL/min; **C.** RECA blood flow 104 mL/min (normal); **D.** RVA with compensatory blood flow increase 258 mL/min; **E.** LICA with no atherosclerotic lesions; **F.** LICA increased compensatory blood flow 657 mL/min; **G.** LECA blood flow 104 mL/min (normal); **H.** LVA blood flow 110 mL/min (normal). Total blood flow 1261 mL/min – the patient requires no intervention, a candidate for conservative treatment

gradually increasing values, which are the basis for determining significant stenosis of more than 50% and 70–80%, as potentially requiring surgical intervention. Currently, EDV of more than 40–50 cm/s is considered a threshold indicating stenosis of >50%. For stenosis of >70%, the PSV/EDV threshold is 230–250/100 cm/s, respectively^(2,5,9–12). Atherosclerotic plaque morphology is a factor influencing the reliability of measurements – calcified lesions with irregular surface may cause both technical difficulties and hemodynamic disturbances not corresponding to the degree of stenosis. Blood flow assessment in the upper vascular segments, 3–4 cm above stenosis, where turbulences due to lumen diameter variations are no longer present, is a valuable guidance. At least a five-fold decrease in PSV velocity indicates stenosis of >70%. Prolonged acceleration time of more than 0.2 seconds, which occurs in stenosis <80%, is an equally important measurement factor in such cases⁽²⁾.

The entire diagnosis of brain-supplying arterial stenosis is currently focused on blood flow velocities assessment in the narrowed intracerebral arteries, ignoring the fact that numerous vessels are involved in blood supply to the brain. These vessels connect, forming a ring-like network of basilar arteries, referred to as the circle of Willis, which can be supplied by either physiological vessels, i.e. the internal carotid arteries and the vertebral arteries, or collateral vessels, predominantly by the branches of the external carotid arteries^(13–16). Only after understanding the mechanisms underlying blood flow compensation, the diverse spectrum of clinical symptoms observed in similar cases of stenosis can be explained.

In this paper, we propose a different course of action as it is not the appearance of blood vessels that determines the intracerebral flow. Blood flow velocity also does not provide complete information. It allows for the assessment of stenotic degree and, owing to the assessment of blood flow in the upper segment of the vessel – decreased velocity and the associated reduction in blood flow – it indirectly provides information regarding decreased intravascular pressure. However, it is impossible to assess brain perfusion on this basis. Our analysis included a group of 218 patients over the age of 60 years, who were referred for intracerebral Doppler evaluation due to suspected stenosis. Two groups with significant intracerebral stenosis of more than 50% (38/44 patients), which differed in terms of the presence of increased blood flow in other vessels, were subject to a detailed analysis. The following changes were reported for the compensatory group:

- increased intracerebral blood flow vs. the non-compensatory group (119 vs 86% of the norm);
- increased number of asymptomatic patients (31/44 – 70% (14/38 – 37% in the non-compensatory group);
- increased number of patients with ICA obstructions (15/5).

Stenosis of any of the brain-supplying arteries (including vertebral vessels) triggers, through unknown mechanisms, an increase in blood flow in all available vessels that can supply the brain. This phenomenon, which is governed by the all-or-none principle, causes a nearly 20% increase in brain perfusion with a simultaneous decrease in the blood flow through the significantly narrowed ICA. The external carotid arteries, which form junctions in the maxillary arteries, are also an equally important route of blood flow to the brain as vertebral arteries. This mechanism depends on individually available vascular connections specific for each patient. The mechanism is also responsible for different behavior of patients after stroke with gradual decrease/resolution of changes in patients with developing collateral blood flow. Owing to this fact, in most cases (70%) patients do not develop clinical symptoms indicating brain ischemia. The three-fold increase in the number of patients with ICA obstructions in the group of patients with increased intracerebral blood flow is the strongest argument to support the importance of compensatory mechanisms.

Conclusions

The presented data should have an immense impact on the management in patients with stenosis of more than 70/80% as well as the introduction of fundamental modifications in the current division into symptomatic and asymptomatic patients. A collateral circulation in an asymptomatic patient with significant ICA stenosis is an argument for the initiation of conservative treatment, whereas asymptomatic patients with significant stenosis, but with no increase in the blood flow in other arteries should be referred for recanalization procedures as massive stroke or death will be the first clinical symptom of stenosis in these patients.

An inclusion of the degree of collateral circulation in the assessment protocol for brain perfusion in patients with significant ICA stenosis may significantly modify the current management strategies for symptomatic and asymptomatic patients, as well as create a plane of understanding between neurologists in favor of conservative treatment and vascular surgeons/vascular radiologists performing surgical interventions, which will in turn allow for the choice of an optimal, patient-tailored method of treatment (Fig. 1, Fig. 2, Fig. 3).

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the content of this publication and/or claim authorship rights to this publication.

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