

CORRELATION OF NEUROLOGICAL SYMPTOMS AND BREATH HOLDING INDEX VALUES IN PATIENTS WITH SEVERE INTERNAL CAROTID STENOSIS

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SUMMARY – The aim of the study was to evaluate the role of cerebral vasoreactivity measurement in the follow up of patients with severe internal carotid stenosis. We used breath holding index (BHI) as a quantitative parameter of cerebral vasoreactivity and functional state of cerebral hemodynamics. We evaluated data of 150 patients with high grade carotid stenosis (definition according to standardized criteria of the Cerebrovascular Laboratory, Reference Center for Neurovascular Disorders of the Ministry of Health of Republic of Croatia). All patients underwent CDFI, TCD and CT/MR imaging tests, complete laboratory work-up, ECG, chest x-ray, and spinal tap in selected cases. CDFI and TCD findings were obtained in a standardized manner. BHI was calculated as percentage increase in mean blood flow velocity (MBFV) occurring during breath holding divided by the time (seconds) for which the subject hold his/her breath. All patients had verified recent ischemia of brain parenchyma on CT/MR scan. There were 29 (19%) symptom-free patients, 14 (9%) men and 15 (10%) women, who had BHI >0.7; 35 (24%) patients, 15 (10%) men and 20 (14%) women, with transient neurological symptoms, without recent ischemic lesions on CT/MR scan and BHI \geq 0.7; and 86 (57%) patients with first ever stroke, 54 (36%) men and 32 (21%) women, who had hemispheric symptoms according to the site of stenosis (BHI <0.7). BHI is an easy and reproducible, real time method in the follow up of patients with severe carotid disease. It is very useful in predicting decompensation of intracranial collateral circulation, hemodynamic insufficiency and cerebrovascular accident.

Key words: *Cerebral arteries – physiopathology; Carotid artery diseases – diagnosis; Carotid stenosis – ultrasonography; Ultrasonography, Doppler, transcranial*

Introduction

According to the results of the European Carotid Surgery Trial (ESCT) and North American Symptomatic Carotid Endarterectomy Trial (NASCET), in the last decades all patients with symptomatic carotid stenosis without other risks for global anesthesia were candidates for carotid endarterectomy. Asymptomatic patients were followed up and usually became candidates for carotid

endarterectomy too late when they had suffered ischemic stroke. Nowadays, according to the results of the Asymptomatic Carotid Surgery Trial (ASCT), asymptomatic patients should be evaluated for surgical risks and long-term benefits from carotid endarterectomy¹⁻³.

Cerebral autoregulation is the ability to maintain constant cerebral blood flow despite changes in the cerebral perfusion pressure. First studies of brain perfusion included measurements performed at different blood pressures, whereas nowadays transcranial Doppler ultrasound (TCD) is used to evaluate dynamic cerebral autoregulation in humans⁴⁻⁶.

Measurement of regional cerebral blood flow (rCBF) by CT Xenon 133 clearance, dynamic susceptibility con-

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trast MR imaging (DSC MRI) or more sophisticated PET and SPECT methods can be performed. Correlation of the results estimated by TCD and the previously mentioned, less available, time consuming and expensive techniques has shown that TCD is an accurate, specific and sensitive method for cerebral flow evaluation⁷⁻¹³. Industrialized countries have higher opportunities than transition countries like Croatia, which cannot introduce such expensive methods in daily practice; in addition, these methods are not reproducible and cannot be used at bedside. Therefore, we tried to find a method that would be sensitive and specific enough, reproducible and bedside available, while also being inexpensive.

Breath holding method has been introduced in the early '90ies as a non-aggressive, well-tolerated, real time, reproducible screening method for studying cerebral hemodynamics. The respective studies were performed in small groups, mostly dealing with examination technique and cut off breath holding index (BHI) values between patients with symptomatic and asymptomatic carotid disease¹⁰⁻¹³. In our previous studies, we standardized this method and BHI values in healthy, cerebral symptom-free different age groups of both sexes.

We have shown the BHI value in normal symptom-free population to be >1 in all individuals⁶. In the present study, we tried to find the cut off values in patients with asymptomatic and symptomatic carotid stenosis to be used in the follow up of these patients, and to identify the right time for surgical treatment.

Subjects and Methods

We evaluated data of 150 patients (83 men, mean age 66±12, and 67 women, mean age 74±10) with unilateral severe carotid stenosis (75%) according to the criteria of the Cerebrovascular Laboratory, Reference Center for Neurovascular Disorders of the Croatian Ministry of Health. Patients were divided according to the site of stenosis into two groups, and symptoms verified on CT scan into two groups, transient ischemic attack (TIA) and stroke. Patients with moderate or severe

Table 1. Number and mean age of patients with occlusive carotid disease

	Men	Women	Pooled
Number of patients	83 (55%)	67 (45%)	150
Age, mean ± standard deviation	66±12	74±10	71±10

Table 2. Number of patients according to site of stenosis

	Men	Women	Pooled
Right ACI	30 (20%)	25 (17%)	55 (37%)
Left ACI	50 (33%)	45 (30%)	95 (63%)

ACI, arteria carotis interna

atherosclerotic changes of the other main head and neck blood vessels were not included in the study. Evaluation of extracranial blood vessels was performed by the Color Doppler Flow Imaging (CDFI) and Power Doppler Imaging (PDI) methods on an Aloka 5500 Prosound, 7.5 MHz linear probe.

The TCD examination was performed on a TCD DWL Multidop X4 instrument with a 2 MHz hand-held pulsed wave Doppler probe, in supine position after 5-minute bed rest. The probe was placed over each transtemporal window, arteries of the circle of Willis were insonated by standard protocol, and mean blood flow velocity (MBFV) values were recorded. Blood vessels of the vertebrobasilar system were insonated by standard protocol through the suboccipital window with the same probe in sitting position.

MBFV of the middle cerebral artery (MCA) was continuously monitored during the breath holding test. BHI was calculated as percentage increase in MBFV occurring during breath holding divided by the time (seconds) for which the subject hold his/her breath in standardized manner, as previously described^{6,8,9}.

$$V_{\max} - V_{\text{mean}} / \text{seconds} \times 100$$

Statistical analysis of different groups of subjects was performed by non-parametric χ^2 and Fisher test (statistical significance was set at $p < 0.05$). Coefficient of variation was calculated for BHI values as a measure of data dispersion for each group.

Results

There was no statistically significant difference in

Table 3. Number of symptomatic and asymptomatic patients in study population

	Men	Women	Pooled
Symptom-free	14 (9%)	15 (10%)	29 (19%)
Transient ischemic attack	15 (10%)	20 (14%)	35 (24%)
Stroke	54 (36%)	32 (21%)	86 (57%)

the number of evaluated men and women; women were 10 years older than men ($p < 0.05$) (Table 1). There was a statistically significant difference in the number of patients according to the site of stenosis, with a prevalence of patients with left carotid artery stenosis in both sexes taken together (63% *vs.* 37%) as well as among men (33% *vs.* 20%) and women (30% *vs.* 17%) in separate (Table 2). There were 29 (19%) symptom-free patients, 14 (9%) men and 15 (9%) women, who had BHI > 0.7 ; 35 (23%) patients, 15 (10%) men and 20 (14%) women, with transient neurological symptoms, CT/MR scan showing no recent ischemic lesions, and BHI ≥ 0.7 ; and 86 (57%) patients with first ever stroke, 54 (36%) men and 32 (21%) women, with hemispheric symptoms according to the site of stenosis (BHI < 0.7) (Table 3).

Discussion

In industrialized countries, stroke is the second cause of death and first cause of disability, whereas in Croatia acute stroke is the leading cause of death and disability. One-fourth of all ischemic stroke cases (25%) are caused by severe stenosis of the main neck blood vessels. In order to reduce stroke incidence we tried to introduce a new screening method in daily cerebrovascular evaluation of stroke risk patients^{6,14-18}. In normal individuals, a fall in the cerebral perfusion pressure does not influence regional cerebral blood flow because of cerebral blood flow autoregulation^{19,20}. These cerebral blood flow compensatory mechanisms are exhausted in pathological conditions with acute cerebrovascular incident as a consequence. Clinical trials suggest that carotid endarterectomy can significantly lower the stroke risk in symptomatic patients as well as in most asymptomatic cases¹⁻³. Previous studies have shown that the measurement of cerebrovascular vasoreactivity provides reliable assessment of the hemodynamic effects of a severe carotid stenosis. BHI proved to be a reliable prognostic factor for assessment of the stroke risk in symptomatic carotid stenosis²¹⁻²⁴. In our study, we showed that there was a cut-off value of BHI in asymptomatic (between 0.7 and 1.0) and symptomatic (below 0.7) patients, and that BHI could be very helpful in the evaluation and follow up of patients with severe carotid stenosis.

This study proved the TCD breath holding method to be a well-tolerated, non-aggressive, reproducible, real-time, bedside screening method for studying cerebral hemodynamics in patients with severe carotid stenosis. There is a special impact of this method on the evalua-

tion of asymptomatic patients, their follow up, and on calculating their surgical risk and benefit from carotid endarterectomy^{1-3,16,25}.

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Sažetak

KORELACIJA NEUROLOŠKIH SIMPTOMA I VRIJEDNOSTI INDEKSA ZADRŽAVANJA DAHA U BOLESNIKA SA ZNAČAJNOM STENOZOM UNUTARNJE KAROTIDNE ARTERIJE

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Cilj ovoga istraživanja bio je utvrditi značenje procjene moždane vazoreaktivnosti u bolesnika sa značajnom stenozom unutarnje karotidne arterije (ACI). Za procjenu stanja moždane vazoreaktivnosti te kvantifikaciju njezine funkcije služili smo se mjerenjem indeksa zadržavanja daha (IZD). U istraživanje smo uključili 150 bolesnika sa značajnom stenozom ACI. Svim bolesnicima je učinjen ekstrakranijski i intrakranijski dopler krvnih žila, snimanje mozga pomoću CT/MR, potpune laboratorijske pretrage, te EKG i RTG torakalnih organa. Sve ultrazvučne pretrage učinjene su prema standardnom protokolu, IZD je izračunat kao postotak porasta vrijednosti srednjih brzina strujanja krvi u srednjoj moždanoj arteriji u mjerenom vremenu. Bilo je 29 (19%) bolesnika bez simptoma, 14 (9%) muškaraca i 15 (10%) žena, koji su imali IZD >0,7, a CT/MR nije pokazao svježih lezija moždanog parenhima; 35 (24%) bolesnika, 15 (10%) muškaraca i 20 (14%) žena, s tranzitornim neurološkim simptomima, u kojih CT/MR nije pokazao svježih lezija moždanog parenhima, a BHI je bio ≥0,7; 86 (57%) bolesnika s prvim moždanim udarom, 54 (36%) muškaraca i 32 (21%) žene, koji su imali dokazanu svježu ishemijsku leziju na CT/MR mozga koja je odgovarala strani stenozu uz kontralateralne neurološke simptome (BHI <0,7). Mjerenje indeksa zadržavanja daha je jednostavna, reproducibilna metoda u stvarnom vremenu koja je vrlo korisna u praćenju bolesnika sa značajnom stenozom ACI. Vrlo je korisna u procjeni trenutka dekompenzacije intrakranijskih kolateralnih puteva te posljedične hemodinamske insuficijencije i ishemijskog infulta.

Ključne riječi: *Moždane arterije – fiziopatologija; Bolesti karotidnih arterija – dijagnostika; Karotidna stenozu – ultrazvuk; Ultrazvuk, Dopplerov, transkranijalski*