

## CEREBROVASCULAR RISK FACTORS - IN VIEW OF STROKE PREVENTION

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**SUMMARY** – Stroke risk factors can be divided into those with evidence-based relationship and those with supposed relationship to ischemic stroke, and into potentially treatable risk factors and risk factors with no therapeutic options. Age, gender and race are risk factors with no therapeutic options, while among treatable stroke risk factors most important are high blood pressure, atrial fibrillation, patent foramen ovale, cardiac disorders, diabetes mellitus, hiperhomocysteinemia, hiperlipidemia, and living conditions such as smoking and heavy alcohol drinking. Data about the use of antioxidant vitamins (A,C,E,) are still controversial as well as the role of infection in the development of atherosclerosis.

**Key words:** *Cerebrovascular accident, etiology; Cerebrovascular accident, prevention and control; Risk factors*

Talking about cerebrovascular risk factors, we have to divide them into risk factors with evidence-based relationship and those with supposed relationship to ischemic stroke. For stroke prevention, differentiation between the potentially treatable risk factors and risk factors with no therapeutic options is especially important.

### No Therapeutic Options

Among risk factors with no therapeutic options, age certainly is the most important independent risk factor. Furthermore, male gender, positive family history, and black or Asian race are associated with an increased stroke risk. There is a positive correlation between stroke mortality and low temperatures as well as with the prevalence of respiratory tract infections. Although these risk factors can hardly be modified, their identification should lead to a screening for other risk factors that can be modified by vigorous treatment.

### Potentially Therapeutic Options

Besides age, high blood pressure certainly is the most important risk factor for stroke, where appropriate antihypertensive therapy quickly leads to a relative risk reduction by up to 40%. This benefit has been demonstrated for all age groups as well as for slightly elevated blood pressure and isolated systolic hypertension. Furthermore, treatment with ACE inhibitors such as ramipril could show some protective effect on vascular walls (HOPE study), in addition to their antihypertensive effect<sup>1-3</sup>.

One third of all ischemic strokes are due to cardiac embolism with atrial fibrillation being the most important underlying cause. There is a positive correlation between atrial fibrillation and age as well as a further increase in stroke risk if there is a history of diabetes, hypertension or congestive heart failure. Treatment with moderate oral anticoagulation (INR 2.0-3.0) lowers the yearly stroke risk by up to 5% with an intracranial bleeding rate of 0.5% and total bleeding rate of nearly 2%. Warfarin has been shown to be more effective than aspirin in the prevention of stroke due to atrial fibrillation, however, the patient's age and an additional risk profile should be considered in the choice of treatment<sup>1,2,4,5</sup>.

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A patent foramen ovale (PFO) can cause stroke *via* paradoxical embolism. The risk of embolization increases with PFO size and prevalence of hypermobile atrial septum or atrial septum aneurysm. Besides platelet inhibitors and oral anticoagulants, surgical and transcatheter closure have been discussed in view of stroke prevention and should be further investigated in case - control studies<sup>6</sup>.

Other cardiac disorders such as sick sinus syndrome, dilatative cardiomyopathy, and those with impaired left ventricular function, e.g., large myocardial infarctions, also are associated with an increased risk of embolic stroke. Oral anticoagulation in view of stroke prevention should therefore be critically considered<sup>1,2</sup>.

Insulin resistance, hyperglycemia, and manifested diabetes mellitus all are independent risk factors for stroke as well, with small and large vessel arteriosclerosis being the consequence of poor metabolic control. Therefore, HbA1c levels below 7% should be achieved according to the UKPD Study, which demonstrated positive relationship between the reduction of stroke risk and well controlled diabetes mellitus<sup>1,2,7</sup>.

Hyperhomocysteinemia has recently also been demonstrated to be associated with arteriosclerosis of large, and especially of small cerebral vessels, thus leading to an increased stroke risk. A daily intake of 5 mg folic acid can lower the blood levels of homocysteine, however, data are still lacking which would show that this can also reduce the stroke risk<sup>8,9</sup>.

The important role of hyperlipidemia as a risk factor for cerebral ischemia has been confirmed many times. Three large studies demonstrated that even in patients with normal cholesterol levels, the intake of statins (shown for simvastatin and pravastatin) reduced the absolute risk of stroke. An LDL-cholesterol level below 100 mg/dl should be achieved<sup>1,2,10-12</sup>.

A history of transient ischemic attack (TIA) increases the stroke risk by up to 20% in the first 6 to 12 months. So, each TIA should be followed by search for the underlying cause. TIAs due to carotid stenosis are especially related to an increased stroke risk. Furthermore, asymptomatic carotid artery stenosis also is associated with an increased stroke risk of approximately 1.3% (stenosis <75%) to 3.3% (stenosis >75%) *per* year. Opinions on conservative management with platelet inhibitors *versus* surgical intervention, e.g., stenting or carotid endarterectomy, are still controversial.

Living conditions are also related to the incidence of stroke. Smoking leads to a dose-dependent increase in stroke risk, whereas smoking cessation is associated with

a rapid decrease in this risk. The role of alcohol consumption is still a matter of controversy and discussion. Heavy alcohol drinking has been clearly demonstrated as a risk factor for intracerebral hemorrhage, while the potentially protective effect of moderate alcohol use awaits to be definitely determined. Data concerning the substitution of antioxidant vitamins (A, C and especially E) are still contradictory, therefore daily vitamin supplementation for stroke prevention cannot yet be recommended<sup>1,2,13</sup>.

Finally, the importance of bacterial and viral infections remains unclear as yet. The role of infective triggers in the development of arteriosclerosis (e.g., *Chlamydia pneumoniae* and others) within the concept of 'pathogenic burden' has yet to be elucidated<sup>14</sup>.

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## SAŽETAK

RIZIČNI ČIMBENICI ZA NASTANAK CEREBROVASKULARNIH BOLESTI  
S OSVRTOM NA PREVENCIJU

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Rizični čimbenici za nastanak moždanog udara mogu se podijeliti na one kod kojih je povezanost s moždanim udarom dokazana i na one kod kojih se ta povezanost pretpostavlja, na one na koje se može terapijski djelovati i one na koje se ne može djelovati. Rizični čimbenici na koje se ne može djelovati su dob, spol, rasa, dok su među onima na koje se može djelovati najvažniji povišen tlak, atrijska fibrilacija, otvoreni foramen ovale, srčani poremećaji, šećerna bolest, hiperhomocisteinemija, hiperlipidemija, te čimbenici povezani s načinom života, kao što su pušenje i prekomjerno pijenje alkohola. Podaci o primjeni antioksidativnih vitamina (A, C i E) još uvijek nisu nedvosmisleni, što također vrijedi i za ulogu upale u nastanku ateroskleroze.

Ključne riječi: *Moždani udar, etiologija, Moždani udar, prevencija i kontrola; Rizični čimbenici*