CURRENT TOPIC

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Metabolic syndrome and restenosis of carotid artery

Metabolički sindrom i restenoza karotidne arterije

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Introduction

Clustering of risk factors for cardiovascular disease has been investigated from the third decade of the 20th century [1–3]. It was named metabolic syndrome (MSy) by World Health Organization in the year 1999 [4]. In 2001, the National Cholesterol Education Program – Adult Treatment Panel III (ATP III) (NCEP-ATP III) proposed both diagnostic criteria for MSy and cut-off points for its components [waist circumference, blood pressure, high-dentsity lipoprotein cholesterol (HDL-C), triglycerides and fasting blood glucose], which are considered acceptable for everyday clinical work [5]. NCEP-ATP III criteria were revised in 2005 by the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) – modified NCEP-ATP III criteria, called also NHLBI-AHA criteria [6]. In 2006 International Diabetes Federation (IDF) recommended a new definition of the MSy – IDF definition [7]. There is no general agreement as to which definition is more suitable for diagnosis of MSy, but it seems that the modified NCEP-ATP III criteria are the most appropriate [8].

According to literature data, the frequency of MSy varies from 9% to 34% depending on studied population and MSy definition which was used in investigation [9–12]. The frequency of MSy is related to age. For example, in the USA population, in subjects more than 60 years old the frequency of MSy was 51.5%, and in subjects 40–60 years old it was 40.8% [10]. MSy is also more frequent in obese [13].

The MSy prevalence is higher in patients with atherosclerotic disease. In a study of Gorter et al [14], which included 1,117 patients aged 18–80 years (mean age 60 ± 10 years) with verified atherosclerotic disease, MSy prevalence, defined according to ATP III criteria, was 46%. There are differences in MSy prevalence depending on the type of atherosclerotic disease. In the above mentioned study of Gorter et al. [14] and in an Olijhoek et al. [15] study the prevalence of MSy was about 58% in patients with peripheral vascular disease, about 41% in patients with coronary disease, 43% in patients with carotid disease and 47% in subjects with abdominal aortic aneurysm.

According to recently published data from a study conducted in Belgrade, the MSy prevalence, defined according to ATP III criteria, was 55.6% in patients with carotid disease [16] and 59.8% in patients with peripheral vascular disease [17].

Carotid artery restenosis

Carotid endarterectomy (CEA) has been proved as successful in prevention of disabling and fatal strokes in patients with asymptomatic and symptomatic carotid diseases [18–20].

CEA is one of the most frequent vascular operations in the USA, with more than 117,000 of this intervention per year [21]. Several large, multicentric controlled trials showed that among carefully selected patients CEA had better effect as stroke prevention than medical therapy [22]. In a study conducted in Belgrade which included a total of 309 symptomatic patients with near total internal carotid artery occlusion, those who underwent CEA had lower incidence of transient ischemic attack, ipsilateral stroke, and neurologic death during follow-up than medically treated patients [23].

After CEA in some patients reccurent carotid stenosis occur. Reviewing over 200 references Lattimer and Burnand [24] found that the overall incidence of symptomatic recurrent stenosis ranged from 0% to 8.2%, and the one of asymtomatic restenosis was between 1.3% and 37%. In a Liapis et

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al. [25] study the incidence of restenosis was 4.0%, all restenosis were asymtomatic, and average time from CEA and occurence of restenosis was 47.4 months.

In a Fluri et al. [26] study, 5 years after CEA, the probability for the ipsilateral progressive carotid disease was 5.2%, and after 15 years, the likelihood was 37%.

Recurrent carotid stenosis higher than 60% the most frequently occurs two years after CEA [27]. Postoperative oclusion develops in about 1% of operated [24, 28].

Risk factors for carotid artery restenosis

Risk factors for restenosis have been investigated in many studies [25, 26, 29–31]. According to Lattimer and Burnand [24], for early restenosis, within 2 years after CEA, risk factors are smoking, lower diameter of carotid artery, some anomalies found during operation and some genetic factors. Cerebrovascular risk factors such are hypertension, hyperlipidemia, diabetes, obesity and smoking are important for progressive restenosis, which occurs at least 2 years after operation. In a study of Reina-Gutierrez et al. [28], the highest risk for serious restenosis had women and subjects with diabetes. In a Volteas et al. [32] investigation, diabetes, ishaemic heart disease, hyperlipidemia and family history of cardiovascular diseases were significantly more frequent in patients with restenosis in comparison with those without restenosis. Rapp et al. [33] found that hypercholesterolemia was related to early restenosis, and that hypertension was related to both early and late restenosis. Association of cerebrovascular risk factors with restenosis has not been proved in any investigations [29–31]. For example, Strineka et al. [34] did not find this association and concluded that restenosis was not caused by cerebrovascular risk factors, but by perioperative complications. One of the reasons for these inconsistencies could be a different number of patients studied and different duration of their follow-up.

In a study of Fluri et al. [35], published in the year 2010, a group of 361 patients with CEA was followed 7 years after operation, out of cerebrovascular risk factors present before operation, smoking, diabetes and hypercholesterolemia were significantly related to progressive restenosis. However, more important were newly acquired cerebrovascular risk factor, that is the factors not present before CEA. Acquisition of at least one new cerebrovascular risk factors (with exception of hypercholesterolemia) significantly increased the risk for progressive restenosis [35].

Metabolic syndrome as a predictor of adverse outcomes after carotid revascularization

It is well known that MSy is associated with cardiovascular diseases. This association has been found in a large number of studies [10, 36, 37]. Compared with persons without MSy, persons with MSy had both increased mortality from cardiovascular diseases (12.0% *vs* 2.2%) and increased total mortality (18.0% *vs* 4.6%) [10]. Whether MSy is associated with restenosis is not known yet.

Since the majority of MSy components have been found to be related to restenosis it could be expected that restenosis is more frequent in patients with MSy. So far, only a study of Protack et al. [38] described the outcomes for patients with MSy after carotid revascularization (carotid endarterectomy and carotid stenting). In a total of 921 patients of which 750 underwent CEA and 171 carotid stenting, 31% were identified as having MSy. During follow-up (on an average of 4.5 years) there were no differences between MSy and No-MSy patients with respect to patency, restenosis, reintervention, or survival. Differences, however, existed for freedom from stroke, myocardial infarction (MI) and major adverse event defined as the occurrence of ipsilateral stroke, MI or death during follow-up MI. In comparison with No-MSy, those with MSy had more frequently perioperative morbidity, stroke, MI and major adverse event. These differences were significant for patients with diabetes, but not in those without diabetes. The authors concluded that a long-term stroke prevention is poor in the presence of MSy and that MSy should be considered as significant risk factor for patients undergoing carotid revascularization.

Conclusion

Although there is no evidence that MSy is a risk factor for carotid restenosis, the fact that a majority of its components are related to restenosis, and finding that stroke prevention is poor in the presence of MSy, suggest that MSy is an important risk factor for adverse outcomes after carotid revascularization.

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