# ROLE OF RISK FACTORS IN PREDICTION OF ASYMPTOMATIC CAROTID ARTERY STENOSIS IN PATIENTS WITH CORONARY ARTERY DISEASE

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***ABSTRACT***

***Aims****: To determine the frequency of asymptomatic carotid artery stenosis in patients with coronary artery disease and to what degree the extent of coronary artery disease and presence of certain risk factors can be indicators of carotid artery stenosis in asymptomatic patients.*

***Material and methods****: Retrospective evaluation of consecutive patients that underwent coronary artery bypass grafting (CABG) during one year without symptoms or signs of carotid artery stenosis. The pre-operative Doppler ultrasonography in color and B-mode, using Siemens Accuson Antares machine, was used to determine the presence and the degree of carotid artery stenosis. Patients were divided according to the presence of significant (≥50%) carotid artery stenosis. The same doctor performed all examinations. Following variables were analysed: age, gender, body mass index, hypertension, diabetes, smoking, cholesterol, triglycerides and echocardiographic variables obtained from transthoracic echocardiography - the presence of aortic wall sclerosis, aortic valve sclerosis and mitral valve calcification.*

***Results****: We have demonstrated that in 18/272 (7.1%) of patients referred to CABG with hemodynamically significant carotid artery stenosis had asymptomatic stenosis. The risk of presence of carotid artery stenosis was more significant in those older than 60 years (OR 2.58; 95% CI 0.98-6.77, p=0.047) and in patients with left main coronary artery stenosis (OR 8.92; 95% CI 3.2-24.83, p<0.001). Other investigated variables had no significant influence (p>0.05).*

***Conclusion****: The presence of asymptomatic carotid artery stenosis is strongly associated with the presence of left main coronary artery stenosis and with age older than 60 years. Noninvasive screening for carotid disease is reasonable in these subgroups of patients referred to CABG.*

***Key words****: Carotid artery stenosis, Left main, Risk factors, Adults, Ultrasonography.*
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## Introduction

Carotid artery atherosclerosis, as one of the signs of generalized atherosclerosis, is frequently associated with coronary artery disease (CAD). The prevalence of hemodynamically significant carotid stenosis in the CAD population ranges from 17% up to 22%[1-4]. Carotid artery stenosis (CAS) tends to be both asymptomatic and symptomatic. Diagnosis of asymptomatic CAS is important not only for isolated carotid artery disease, but also as an accompanying diagnosis in other conditions that require surgical management (cardiovascular surgery, extensive abdominal surgery, orthopedic surgery, transplantation of different organs, etc), for it can seriously compromise peri-operative success if it goes undetected. Intraoperative hypotension and great variations in cerebral perfusion that are associated with coronary surgeries in the presence of CAS, can predispose to the occurrence of stroke[5,6]. Perioperative risk for stroke increases with the increase of the degree of carotid stenosis and ranges from <2% for stenosis <50%, 10% for stenosis of 50-80% and 11-18.8% for stenosis over 80%[7,8].

Strokes usually occur between Day 2 and Day 9 post-operatively.

Joint asymptomatic CAS and CAD is of special interest for cardiologists and cardiac surgeons given the fact that coronary artery bypass grafting (CABG) is one of the most frequent procedures and that carotid stenosis cause 30% of all post-CABG strokes (9). Perioperative stroke is one of the most severe complications of CABG and is the second cause of overall post-procedural mortality, after the low cardiac output (10). Therefore, early detection of asymptomatic CAS in CAD patients is of paramount importance equally for diagnosis, treatment strategy and prognosis.

The aim of this study was to determine the frequency of asymptomatic CAS in CAD patients and to assess to what degree the extent of CAD and presence of certain risk factors can be indicators of carotid artery disease in asymptomatic patients.

## Materials and methods

The study has been approved by the Ethics Committee of Clinical Center of Serbia and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

This was a retrospective study of patients who underwent CABG in our center. The pre-operative battery of tests included also Doppler ultrasonography of the carotid arteries. By systematic review of all consecutive patients who underwent CABG during a 12 month period, patients who presented no symptoms or signs of carotid artery stenosis were selected. The internal carotid arteries were scanned with carotid duplex equipment. Lesion severity was defined as the greatest stenosis observed either on the right or left internal carotid artery. A significant carotid artery stenosis was defined as ≥50% of diameter stenosis, while stenosis <50% were considered hemodynamically non-significant[11].

In our experience ultrasound findings match surgical findings (when the level of carotid artery stenosis is concerned). Color Doppler ultrasound of carotid arteries determines with great certainty the true level of stenosis. Being that we are country in transition with limited resources, it is not always possible to perform more expensive diagnostic procedures such as computed tomography (CT) or magnetic resonance imaging (MRI). Coronary angiography was performed by standard techniques and the severity of coronary lesions was determined visually. Stenosis of ≥70% in major epicardial arteries or 50% for the left main coronary artery were defined as clinically significant[12].

All categories of patients were analysed for frequency of asymptomatic CAS and for the impact of risk factors (age, gender, family history of CAD, smoking, presence of hypertension, diabetes, dyslipidemia and obesity) on the prediction of CAS. Also, the presence of 3 parameters on trans-thoracic echocardiography examination (aortic wall sclerosis, aortic valve sclerosis and mitral valve calcification) were evaluated.

Statistical analysis was performed using the methods of descriptive statistics: central tendency measures (mean), measures of variability (interval variations max-min, standard deviation SD), relative numbers, as well as the method of analytical statistics; methods for the identification of empirical distribution functions, methods to test the significant difference (Student's T test, $\chi 2$ test, one-way ANOVA), and method for the evaluation of significant difference (Pearson's coefficient of correlation r, Spearman's rank coefficient $\varrho$ and univariate logistic regression analysis).

## Results

All 942 consecutive patients who underwent CABG during one year were analysed and 272 patients without symptoms or signs of carotid artery stenosis were evaluated, i.e. no previous cerebrovascular incidence (TIA or stroke). Average age was 57.94±9.24 yrs (ranging presented no 31-81 years). Asymptomatic CAS that was hemodynamically significant was present in 18 patients (7.1%).

Patients with hemodynamically significant asymptomatic CAS were older (62.76±7.14 vs. 57.56±9.29; p=0.024) and the risk of presence of hemodynamically significant asymptomatic CAS was more significant in those over 60 years, than in younger patients (OR 2.58, 95% CI 0.98-6.77; p=0.047).

In the entire group, the male gender was predominant (217/272; 79.8%), among those with hemodynamically significant (12/18; 66.7%) and as well as among those with non-significant (205/254; 80.7%) asymptomatic CAS. Between the last two groups, no statistical significance was observed (p=0.131).

Analysing the presence of risk factors for atherosclerosis (hypertension, diabetes, dyslipidemia, obesity, smoking, family history) and echo-parame-

ters that indicate the presence of atherosclerosis (aortic wall sclerosis, aortic valve sclerosis and mitral annular calcification), no statistical significance was found between the two groups either (Table 1).

| Risk factors | Patients with hemodynamically non-significant asymptomatic CAS (n=254) | | Patients with hemodynamically significant asymptomatic CAS (n=18) | | p |
|---|---|---|---|---|---|
| | *Number* | *Percent* | *Number* | *Percent* | |
| HTA | 201 | 79.1 | 15 | 83.3 | 0.472 |
| DM | 49 | 19.3 | 6 | 33.3 | 0.131 |
| Cholesterol | 236 | 92.9 | 18 | 100 | 0.28 |
| LDL cholesterol | 246 | 96.9 | 18 | 100 | 0.574 |
| Triglicerides | 173 | 68.1 | 14 | 77.8 | 0.284 |
| BMI>30 | 49 | 19.3 | 4 | 22.2 | 0.479 |
| Smoking | 153 | 60.2 | 13 | 72.2 | 0.227 |
| Family history | 146 | 57.5 | 13 | 72.2 | 0.164 |
| Aortic wall sclerosis | 218 | 85.8 | 15 | 83.3 | 0.492 |
| Aortic valve sclerosis | 64 | 25.2 | 8 | 44.4 | 0.07 |
| Mitral annular calcification | 58 | 22.8 | 4 | 22.2 | 0.608 |

**Table 1**: Risk factor distribution according to the degree of carotid stenosis.
*CAS- carotid artery stenosis; HTA-hypertension; DM-diabetes mellitus; BMI-body mass index*

All patients with hemodynamically significant asymptomatic CAS had a multi-vessel disease, while in the group of hemodynamically non-significant asymptomatic CAS, 10.2% of patients had single vessel disease (Table 2).

| Coronary artery disease | Patients with hemodynamically non-significant asymptomatic CAS (n=254) | | Patients with hemodynamically significant asymptomatic CAS (n=18) | | p |
|---|---|---|---|---|---|
| | *Number* | *Percent* | *Number* | *Percent* | |
| **One vessel disease** | 26 | 10,2 | - | - | 0.154 |
| **Multivessel disease** | 228 | 89,8 | 18 | 100,0 | |
| **LM stenosis** | 18 | 7.1 | 8 | 44.4 | <0.001 |

**Table 2**: Distribution of coronary artery stenosis depending of the degree of hemodynamically significant carotid stenosis.
*CAS- carotid artery stenosis; LM- left main*

There is no statistical significance in the difference of presence of single and multi-vessel CAD in patients with and without hemodynamically significant carotid stenosis (p=0.154). However, there was a statistical significance in the presence of left main coronary artery stenosis (p<0.001): patients with hemodynamically significant carotid stenosis showed left main coronary artery stenosis more frequently than patients lacking hemodynamically significant carotid stenosis. The risk for significant CAS in patients with left main coronary artery stenosis was higher than in patients without left main coronary artery stenosis (OR 8.92, 95% CI 3.2-24.83; p<0.0001).

## Discussion

In our study asymptomatic CAS that was hemodynamically significant was present in 18 (7.1%) patients who underwent CABG. The risk for presence of CAS was more significant in those older than 60 years and in patients with left main coronary artery stenosis.

The prevalence of severe asymptomatic CAS in the general population ranges from 0% to 3.1%[13]. Atherosclerosis is a diffuse process that involves vessel structures, frequently the carotid and coronary arteries. Hemodynamically significant carotid stenosis is one of the main risk factors for stroke after CABG[14]. Previous postmortem[15] and clinical[1-3,16,17,18] studies have reported a variable prevalence of concomitant carotid and coronary artery disease. In a recently published large study of the patients with CAD, carotid disease was found in 12.8% of patients and severe CAS in 4.6% of patients[19].

In patients scheduled for CABG with previous transient ischemic attack or stroke and a significant carotid stenosis, carotid revascularization is recommended in conjunction with CABG (Guidelines Class IIa, level of evidence C)[20]. It is also recommended in patients with no history of transient ischemic attack or stroke in the presence of bilateral severe carotid stenosis with a contralateral occlusion (Guidelines Class IIb, level of evidence C). Although there are different views[21] on the influence of asymptomatic CAS (stenosis greater than 50% at the level of bifurcation of carotid artery and proximal internal carotid artery in patient without the symptoms of cerebral ischemia) on the development of stroke, most authors agree that the presence of significant CAS in an asymptomatic patient is an independent predictor of a stroke risk immediately after coronary bypass[22-26].

The question on who should undergo carotid screening is still not completely resolved[27,28],

whether it should be done for all or specific groups of patients scheduled for CABG. The presence or absence of a cervical bruit is poorly predictive of a high-grade stenosis even in the setting of a known symptomatic CAD[29]). That's why it is important to identify preoperative risk known to be associated with the presence of carotid artery disease which could stratify patients in high- and low-risk categories.

In our group of patients with CAD analysing the risk factors for atherosclerosis (hypertension, diabetes, dyslipidemia, obesity, smoking, family history) and echo-parameters that indicate the presence of atherosclerosis (aortic wall sclerosis, aortic valve sclerosis and mitral annular calcification), we found none to be a potential predictor of internal CAS.

In this group of patients referred to CABG the male gender was more frequent both in the group with symptomatic and in the group with asymptomatic CAS, but gender was not a predictive factor for CAS. Some studies showed predictive value of the female gender[4,9,30], the others did not confirm this[31]. Other studies showed peripheral vascular disease, previous transient ischemic attack or stroke and smoking, as well as the female gender, as markers associated with important carotid stenosis[32].

Our patients with hemodynamically significant asymptomatic CAS were older than patients without CAS and the risk of presence was more significant in those over 60 years, than in younger patients. Other investigators also found that the prevalence of CAS increases with age. Previous studies have reported a direct correlation between the extent of CAD and the presence of CAS among patients referred for coronary angiography[16,19,27].

In this study we found a strong correlation between asymptomatic CAS and presence of left main stenosis (the risk for CAS was 8.92 times greater) and no correlation with the extent of coronary disease and asymptomatic CAS.

This study is one of few studies which investigated patients with coronary artery disease that have no symptoms of carotid disease. We found that the presence of asymptomatic carotid stenosis is strongly correlated with the presence of left main coronary artery stenosis and with the age older than 60. Although the number of patients with asymptomatic carotid stenosis who had hemodynamically significant left main coronary artery stenosis was small (18 patients), we think, until further research is done, that noninvasive screening for carotid disease is reasonable in these subgroups of patients with coronary artery disease referred for CABG. Also, although we found no correlation with multivessel disease, and as reports in literature are not uniform, until further investigations, screening is reasonable in patients older than 60 years of age and with multiple risk factors.

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