#### Clinical Science

## PREVALENCE OF CAROTID ARTERY DISEASE IN PATIENTS WITH METABOLIC SYNDROME

Tatjana Deleva-Stoshevska<sup>1</sup>

<sup>1</sup> City General Hospital "8th September", Skopje, Republic of North Macedonia

#### **Abstract**

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**Key words:** carotid artery disease, cerebrovascular insult, transient ischemic attack, metabolic syndrome.

\*Correspondence: Tatjana Deleva-Stoshevska. City General Hospital "6th September", Skopje, Republic of North Macedonia E-mail: deleva\_tatjana@ vahoo.com

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There is a growing body of scientific evidence on the impact of metabolic syndrome (MetS) on the progression of atherosclerosis, imposing the need for research of the association of MetS with carotid artery disease (CAD) as a significant risk factor for cerebrovascular insult (CVI) and transient ischemic attack (TIA). The aim of the study was to determine the prevalence of CAD as a risk factor for CVI and TIA in subjects with MetS. Material and methods: A cross-sectional study was performed including a total of 118 subjects, 65 men, 53 women, with MetS according to NCEP ATP III criteria that were analyzed clinically, biochemically and ultrasonographically in the City General Hospital "8th September" - Skopje in the period from January 2017 to January 2018. Waist circumference, blood pressure, glycemia, triglycerides, and HDL cholesterol were determined according to standard routine protocols. The evaluation of the extracranial carotid trunk was done with a Color Doppler Duplex sonography with a linear probe of 7.5MHz. CAD assessment was performed using Ultrasound Consensus Criteria for Carotid Stenosis. An objective neurological assessment of the existence of CVI and TIA was performed by a standard protocol for neurological examination and brain CT results from medical history were reviewed. Results: The prevalence of CAD in this study was 77 subjects (65.25%), of which 35 subjects (29.66%) had symptomatic CAD, 17 subjects (48.57%) had CVI, 18 subjects (51.43%) had TIA. Regarding the degree of carotid artery stenosis (CAS) in the total number of subjects with MetS and CAD, no subjects with normal findings were registered, 16 subjects had stenosis <50%, 29 subjects had stenosis 50-69%, 23 subjects had stenosis 70-99%, while 9 subjects had occlusion. Conclusion: The results obtained in this study have shown that asymptomatic CAD is dominant in patients with MetS, which further imposed the need for timely extracranial ultrasonographic evaluation of the carotid trunk. This would achieve both effective prevention and adequate treatment of CVI and TIA, thereby reducing morbidity and mortality from cerebrovascular events which has a great health and socioeconomic significance.

Клнички истражувања

# КЛИНИЧКИ КАРАКТЕРИСТИКИ НА КОВИД-19 КАЈ ДЕЦАТА ВО ИНСТИТУТОТ ЗА БЕЛОДРОБНИ БОЛЕСТИ КАЈ ДЕЦАТА-СКОПЈЕ

Татјана Делева Стошевска<sup>1</sup>

🗓 Градска ойшīџа болница "8-ми Сейгиември", Скойје, Рейублика Северна Македонија

#### Извадок

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**Клучни зборови:** каротидна артериска болест, цереброваскуларен инсулт, транзиторна исхемична атака, метаболички синдром.

\*Кореспонденција: Татјана Делева Стошевска, Градска општа болница "8-ми Септември", Скопје, Република Северна Македонија. E-mail: deleva\_tatjana@yahoo.com

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Печатарски права: ©2020 Татјана Делева Стошевска. Оваа статија е со отворен пристап дистрибуирана под условите на нелокализирана лиценца, која овозможува неограничена употреба, дистрибуција и репродукција на било кој медиум, доколку се цитираат оригиналниот(ите) автор(и) и изворот.

**Конкурентски интереси:** Авторот изјавува дека нема конкурентски интереси.

Расте бројот на научни докази за влијанието на метаболичкиот синдром (MetS) врз прогресијата на атеросклерозата, што ја наметнува потребата за истражувања на поврзаноста на MetS со каротидна артериска болест (CAD) како значаен ризик-фактор за цереброваскуларен инсулт (CVI) и транзиторна исхемична атака (TIA). Целта на овој труд беше да се утврди преваленцијата на CAD како ризик-фактор за CVI и TIA кај испитаниците со MetS. Материјал и методи: Ова е студија на пресек во која беа вклучени 118 испитаници, 65 мажи, 53 жени, со MetS согласно NCEP ATP III критериумите. Пациентите беа анализирани клинички, биохемиски и ултрасонографски во ГОБ "8-ми Септември" - Скопје во периодот од јануари 2017 до јануари 2018 година. Согласно стандардните рутински протоколи беа одредувани вредностите за обемот на половината, крвниот притисок, гликемијата, триглицеридите и HDL холестеролот. Евалуацијата на екстракранијалното каротидно стебло беше правена со Color Doppler Duplex сонографија со линеарна сонда со фреквенција од 7,5 MHz. Проценката на CAD беше направена со користење на ултразвучни консензус критериуми за каротидна стеноза. Објективната невролошка проценка за постоење на CVI и TIA се вршеше со невролошки преглед по стандарден протокол и со резултатите од КТМ од медицинската историја. Резултати: Вкупната преваленција на CAD кај сите испитаниците со MetS во оваа студија беше 77 испитаници (65,25%); од нив симптоматска CAD имаа 35 испитаници (29,66%) од кои 17 испитаници (48,57%) беа со CVI, а 18 испитаници (51,43%) беа со ТІА. Во однос на степенот на каротидна артериска стеноза (CAS) кај вкупниот број испитаници со MetS и CAD не беа регистрирани испитаници со нормален наод; 16 испитаници имаа стеноза < 50%, 29 испитаници имаа стеноза 50-69%, 23 испитаници имаа стеноза 70-99%, додека, пак, оклузија имаа 9 испитаници. Заклучок: Резултатите од оваа студија покажаа доминација на асимптоматска САD кај испитаниците со MetS, со што дополнително се наметнува потребата за навремена екстракранијална ултрасонографска евалуација на каротидното стебло. Со тоа би се постигнала ефикасна превенција и адекватен третман на CVI и TIA, намалување на морбидитетот и морталитетот од цереброваскуларни настани што има големо здравствено и социоекономско значење.

### Introduction

The influence of the metabolic syndrome on the progression of atherosclerosis has been confirmed in the results of numerous studies, which have also shown a correlation between carotid atherosclerosis and generalized atherosclerosis. Because of this, subjects with MetS are at an increased risk of developing carotid artery disease, cardio and cerebrovascular disease, diabetes mellitus<sup>1</sup>. The underlying pathophysiology of MetS is obesity and insulin resistance, but it is more complicated and involves a number of other factors, including genetic and environmental factors<sup>2</sup>. Carotid artery disease (CAD) involves changes in the arterial wall that cause IMT to thicken, narrow or completely obstruct the carotid artery lumen. Atherosclerosis is the most common cause of CAD. Other non-atherosclerotic causes are rare and include carotid dissection, fibromuscular dysplasia, arteritis (Takayasu), radiation, glomerular tumors on bifurcation, and trauma<sup>3</sup>. That is why atherosclerotic extracranial CAD is included in this study. Selection sites for CAD are carotid bifurcation, the ACI ostium, including the posterior outer wall of the carotid sinus and the distal part of common carotid artery. CAD can be asymptomatic and symptomatic. Asymptomatic CAD is without clinical manifestation of brain suffering, whereas symptomatic CAD may manifest clinically as TIA or CVI. CVI is a medical condition in which poor blood flow to the brain results in the death of cells by initiating an ischemic cascade. TIA is a brief episode of neurological dysfunction with vascular cause, with clinical symptoms usually lasting less than an hour and without imaging evidence of infarction<sup>4</sup>. Disorders phenomenology at CVI and TIA depends on which part of the brain is affected by ischemic suffering.

The aim of the study was to determine the prevalence of CAD as a risk factor for CVI and TIA in subjects with MetS.

## Material and methods

This cross-sectional study comprised a total of 118 subjects with MetS according to NCEP ATP III (National Cholesterol Education Program, Adult Treatment Panel III) criteria, aged  $\geq$  30 and  $\leq$  80 years, that were analyzed clinically, biochemically and ultrasonographically in the City General Hospital "8th September" - Skopje in the period from January 2017 to January 2018.

NCEP ATP III criteria - having any of the three or more of the following parameters:

- 1. Abdominal obesity increased waist circumference values ≥ 102 cm (40 in), women ≥ 88 cm (35 in);
- 2. Increased triglycerides ≥ 150 mg/dL (1.69 mmol/L), or treatment for elevated triglycerides (e.g. fibrates or nicotinic acid);
- 3. Decreased HDL cholesterol values for men <40 mg/dL (1.03 mmol/L), women <50 mg/dL (1.29 mmol/L), or medication treatment for lower HDL cholesterol levels (e.g. fibrates or nicotinic acid);
- 4. Elevated blood pressure values: systolic ≥ 130 mmHg and / or diastolic ≥ 85 mmHg; or treatment with hypertension medications;
- 5. Elevated fasting blood glucose values ≥ 100 mg/dL (5.6 mmol/L); or treatment with antidiabetic drugs.

Inclusion criteria: people with MetS according to NCEP ATP III criteria, age ≥ 30 and ≤ 80 years. Exclusion criteria: individuals without MetS, pregnant women, nursing mothers, age <30 and >80. All participants were informed about the purpose of the research and an informed consent was obtained prior to the study.

MetS assessment was performed according to NCEP ATP III (National Cholesterol Education Program, Adult Treatment Panel III). Waist circumfer-

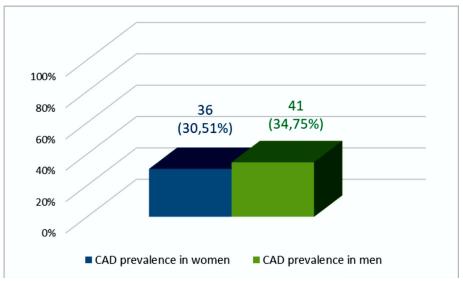
ence was measured at the end of the slow expirium with a soft, elastic band in the upright position of the subject at the midpoint between the upper edge of the iliac bone and the lower edge of the last rib. A mean of two blood pressure measurements with a standard sphygmomanometer was used after a short rest in the sitting position. In the main laboratory of CGH "8th September" - Skopje, venous blood samples were taken after an all-night starvation to assess the following parameters: fasting glycemia, triglycerides and high-density lipoprotein cholesterol (HDL-C). An objective neurological assessment of the existence of CVI and TIA was performed by a standard protocol for neurological examination and brain CT results from medical history were reviewed. CAD evaluation was performed by an ultrasound scan of the extracranial carotid arteries with an Esaote MyLab <sup>™</sup> 70 XVG, with a linear probe with a transmission frequency of 7.5 MHz, using B-mode, color and Doppler mode. CAD assessment was performed using Ultrasound Consensus Criteria for Carotid Stenosis: I. Absence of Stenosis (Normal Finding) - No Plagues, Normal IMT, PSV<125 cm/s, ACI/ACC Ratio of PSV <2, EDV <40 cm/s; 2. II Stenosis <50%: present plaque <50%, IMT thick,

PSV <125 cm/s, ACI/ACC ratio of PSV <2, EDV <40 cm/s; III Stenosis <50-69%: IMT thick, visible plaque> 50%, PSV 125-230 cm/s, ACI/ACC ratio of PSV 2-4, EDV 40-100 cm/s. IV Stenosis 70% to subocclusive (up to 99%): visible narrowing > 50%, PSV> 230 cm/s, ACI/ACC ratio of PSV> 4, EDV> 100 cm/s; V Subocclusion/near occlusion: significant visible narrowing; nearly occluded artery. PSV may be low or no detectable, ACI/ACC ratio of PSV variable, EDV variable; VI Occlusion: no flow, lumen visible, PSV no flow, undetectable, ACI/ACC ratio of PSV not applicable, EDV not applicable.

The statistical analysis of data was performed with the statistical program SPSS for Windows, 23.0. To compare the groups of subjects, the parameter tests (t-test for independent samples, analysis of variance) were used.

### Results

The overall prevalence of CAD among subjects with MetS in this study was 77 subjects (65.25%), The overall prevalence of CAD in terms of gender distribution was 36 women (30.51%) and 41 men (34.75%) (Figure 1). Gender distribution showed no statistical significance (p = 0.24).



**Figure 1.** Distribution of CAD by demographics of the study subjects

Of the total number of subjects, 35 subjects (29.66%) were with symptomatic CAD of which 17 subjects (48.57%)

had CVI, 18 subjects (51.43%) had TIA, and the remaining 42 subjects (35.59%) were asymptomatic.

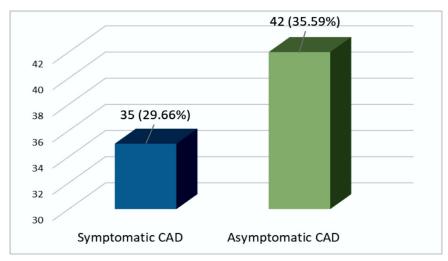
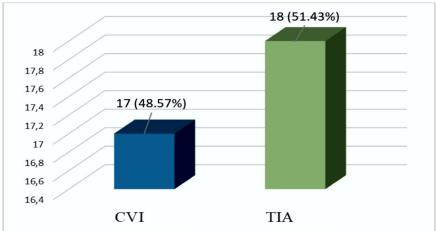


Figure 2. Prevalence of symptomatic and asymptomatic CAD



**Figure 3.** Prevalence of CVI and TIA in symptomatic CAD

Regarding the degree of carotid artery stenosis (CAS) in the total number of subjects with MetS and CAD, there were no reported subjects with normal findings, 16 subjects had stenosis <50%, 29 subjects had stenosis 50-69%, 23 subjects had stenosis 70-99%, and 9 subjects had occlusion (Table1).

Degree of carotid artery stenosis (CAS) in the total number of subjects with MetS and CAD	(n) Number of patients
< 50%	16
50-69%	29
70-99%	23
Occlusion	9

**Table 1.** Degree of carotid artery stenosis (CAS) in symptomatic CAD

#### Discussion

Due to the rise in the prevalence of MetS as a worldwide phenomenon and the increase in morbidity and mortality from cardio- and cerebrovascular disease, numerous been studies have performed establish the correlation to and between MetS cardioand cerebrovascular events. The results of these studies showed a clear and strong association between them. According to the study by Gorter et al., the prevalence of MetS was 41% in subjects with coronary heart disease, 43% with cerebrovascular diseases, and 58% in patients with peripheral arterial disease5. Namely, the results of the study by Ninomiya JK et al. Has indicated a strong, consistent association of MetS with prevalence of myocardial infarction stroke6. The association between generalized atherosclerosis and carotid atherosclerosis and its major influence on the occurrence of cerebrovascular events has also been confirmed and known. Symptomatic implies the etiological association of CAD with TIA and CVI. This is especially important since more than 80% of all strokes are ischemic strokes and only 20% are intracerebral haemorrhage. Of all ischemic strokes, three-fourths occupy the anterior circulation. while one-quarter of the posterior cerebral circulation accounts for the rest of ischemic strokes7. Namely, about 20 - 25% of stroke patients have confirmed atherosclerosis of the large blood vessels in the neck that feed the brain, of which 85% are with CAD as a cause. There is a particularly increased risk of stroke in atherosclerotic stenotic lesions in the extracranial internal carotid arterv or carotid bifurcation8. Similar results were obtained in our

study; the overall prevalence of CAD among MetS subjects in this study was 65.25%, of which 29.66% had symptomatic CAD of which 48.57% had CVI, 51.43% were with TIA, and the rest were asymptomatic.

The prevalence of CAD varies with considerably age on race. For all races the most important factor in the development of CAD is the increasing age. This has been confirmed by several studies, including the Los Angeles County General Hospital study9 and the Caron B. Rockman et al. study10. The results obtained from numerous CAD prevalence studies depend on the criteria applied, the research tools used, and the population covered. Thus, the prevalence of a significant carotid artery stenosis (50% ultrasound-diagnosed carotid stenosis) in the Framingham study was 9% in men and 7% in women11. The highest prevalence was reported in people with acute stroke (60%), then 18% in people with heart disease and 11% in people at increased risk atherosclerosis12. There are numerous studies on the prevalence of moderate carotid stenosis that showheterogeneousdataonadultand gender distribution. However, most of them show that the prevalence of moderate carotid stenosis is higher in men than in women and that the prevalence increases with age in both men and women13-16. In our study, similar results were found for the prevalence of CAD according to gender distribution that was higher in men than in women (34.75% vs. 30.51%). Regarding the degree of stenosis in symptomatic CAD, no subjects with normal findings were registered, 16 subjects had stenosis <50%, 29 subjects had stenosis 50-69%, 23 subjects had stenosis 70-99% , and 9 subjects had occlusion.

## Conclusion

The results obtained in this study have shown that asymptomatic CAD is dominant in patients with MetS, which further imposes the need for timely extracranial ultrasonographic evaluation of the carotid trunk. This would achieve both effective prevention and adequate treatment of CVI and TIA, thereby reducing morbidity and mortality from cerebrovascular events which has a great health and socioeconomic significance.

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