Relationship between Abdominal Obesity and Other Cardiovascular Risk Factors: Cross Sectional Study of Patients with Symptomatic Carotid Disease

Miloš Maksimović, Hristina Vlajinac, Djordje Radak, Jelena Marinković, Jadranka Maksimović, Jagoda Jorga

1Institute of Hygiene and Medical Ecology, School of Medicine, University of Belgrade, Belgrade, Serbia; 2Institute of Epidemiology, School of Medicine, University of Belgrade, Belgrade, Serbia; 3Dedinje Cardiovascular Institute, Belgrade, Serbia; 4School of Medicine, University of Belgrade, Belgrade, Serbia; 5Institute of Medical Statistics and Informatics, School of Medicine, University of Belgrade, Serbia

SUMMARY

Introduction Obesity, particularly visceral obesity, is considered one of major risk factors for cardiovascular events.

Objectives The aim of the present study was to investigate relationship between abdominal obesity and other cardiovascular risk factors.

Methods The cross-sectional study involved 657 consecutive patients with verified carotid atherosclerosis. Carotid atherosclerosis was estimated by high resolution B-mode ultrasonography. Abdominal obesity was defined as waist circumference >102 cm in men and >88 cm in women.

Results Abdominal obesity was present in 324 (49.3%) participants. Multivariate analyses showed that abdominal obesity was significantly positively associated with female sex, increased Baecke’s Work Index of physical activity at work, years of school completed <12, metabolic syndrome, increased triglycerides, hyperglycemia and high serum uric acid. Smoking, alcohol consumption, physical inactivity, hypertension, increased total cholesterol, increased HDL and LDL cholesterols, increased high sensitive C-reactive protein, increased fibrinogen, anti-lipid therapy and anti-diabetic therapy were not significantly related to abdominal obesity.

Conclusion Abdominal obesity among patients with symptomatic carotid disease is significantly related to other cardiovascular risk factors, especially metabolic syndrome, metabolic syndrome components and high level of serum uric acid.

Keywords: abdominal obesity; carotid disease; risk factors

INTRODUCTION

Obesity has become a public health problem in many countries over the several past decades, followed by many clinical and public health consequences [1]. According to the World Health Organization (WHO), on the basis of body mass index (BMI), more than 1 billion adults worldwide are overweight, of whom 300 millions are obese. If the current trend continues, this number will increase to 1.5 billion by 2015 [2]. In 2006, in Serbia every second person among those aged >20 years had BMI >25 kg/m², of whom 36.2% was overweight and 18.3% obese [3].

As well known, obesity is positively associated with increased risk for atherosclerotic disease [4] including stroke [5]. Some investigations have suggested that atherosclerosis is not related to general obesity expressed by BMI, but to abdominal obesity measured by waist circumference (WC) or waist/hip ratio [6,7]. Although BMI is usually correlated with waist circumference, people with identical BMI can have a different distribution of body fat. Waist circumference, which can be easily measured, has been established as a leading anthropometric parameter for measuring the intraabdominal fat depot. According to many investigators, it was found to be a better indicator of obesity and health risks, especially for atherosclerotic disease and type 2 diabetes, than BMI [8,9], and was included as a component of metabolic syndrome (MetS).

OBJECTIVE

The aim of the present study was to investigate relationship between abdominal obesity, expressed by waist circumference and other atherosclerotic risk factors in patients with symptomatic carotid atherosclerotic disease.

METHODS

This cross-sectional study involved 657 consecutive patients with verified carotid atherosclerotic disease who were referred to the Vascular Surgery Clinic Dedinje in Belgrade during the period April 2006 – November 2007. The study included subjects who had symptoms of cer-
Abdominal obesity and carotid stenosis of ≥50%, according to the criteria of North American Symptomatic Carotid Endarterectomy Trial (NASCET) [10]. Carotid atherosclerosis was estimated by high resolution B-mode ultrasonography HDI, ATL 3500.

Exclusion criteria were <18 years of age, malignant disease, previous endarterectomy or rheumatoid arthritis.

Anthropometric parameters and data on cardiovascular risk factors were collected in all participants.

Waist circumference was measured at the midway between the lower ribs and iliac crest. According to WHO criteria patients with abdominal obesity were defined as those with WC >102 cm (men) and >88 cm (women) [11].

Blood pressure was measured using the method recommended by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [12]. The cut-off point was ≥130/130 or ≥85/<85 mm Hg.

To estimate metabolic parameters, fasting plasma glucose (FPG) and lipoproteins, blood samples were obtained after an overnight fast and avoidance of liquids. Levels of fasting plasma glucose (FPG), total cholesterol (TC), serum triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and serum uric acid level were estimated using commercial kits (Abbot, IL,USA) on an automated analyzer (AEROSET™, Abbot, IL, USA). Levels of high sensitivity C-reactive protein (hsCRP) and fibrinogen were measured by using Immunoturbidimetric Fixed Time test (Olympus Diagnostics, O’Callaghan’s Mills Co. Clare, Ireland), and high value of hsCRP was detected according to the CDC recommendations (≥3 mg/L) [13].

Metabolic syndrome (MetS) was defined according to NCEP III criteria [14]. The patients were classified as having metabolic syndrome if they fulfilled 3 or more of the following criteria: 1) triglycerides ≥1.69 mmol/L; 2) HDL-C <1.03 mmol/L (men) and <1.29 mmol/L (women); 3) systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg or antihypertensive drug therapy; 4) obesity, defined as waist circumference >102 cm (men) and >88 cm (women); and 5) abnormal glucose metabolism defined as fasting glucose ≥6.11 mmol/L.

Data on formal educational status, smoking habit and physical activity of study participants were collected by the use of questionnaire.

The cut-off point for educational level was ≤12/>12 years of schooling.

In terms of smoking, participants were divided into never/ever smokers. According to alcohol consumption each patient was classified as drinker (former or current) or non-drinker [15].

Physical activity was assessed in two ways:

1. Physical activity was defined as any type of non-occupational physical exercise for more than 30 minutes per day, during the previous month. Classification of participants in physically active and inactive group was based on the cut-off level of ≤1 per week/>1 per week.

2. Baecke's questionnaire [16] was used for assessing work, sport and leisure physical activity of each participant.

**Statistical analysis**

Continuous variables were described as means ± standard deviation (SD), and categorical variables were presented by counts and percentages. In the analysis of data univariate and multivariate logistic regression analyses were used. All variables which were associated with abdominal obesity at significance level of p≤0.1 were included in the model of multivariate logistic regression analysis. Formal detection of collinearity between independent variables was produced by using Variance Inflation Factor (VIF) which represents the amount of inflation in the variance when the collinearity of a variable with others exists. Criterion used was that with VIFs >2.0 the logistic regression model can lead to inflated standard errors [17]. If collinearity existed the approach to drop one of the correlated variables from the logistic regression model was established in order to reduce multicollinearity.

Data were analyzed using SPSS package version 15 with significance level set at p<0.05.

The study was reviewed and given ethical approval by the Ethics Committee at the University School of Medicine in Belgrade. All patients gave written, informed consent.

**RESULTS**

Of 657 patients, 324 (49.3%) had abdominal obesity. Patients with and without abdominal obesity did not significantly differ either in the degree of carotid stenosis or in the degree of its clinical manifestation (Table 1).

Abdominal obesity was significantly more frequent in women than in men. Patients with abdominal obesity had significantly higher education level, and patients without obesity significantly more frequently consumed alcohol (Table 2). The compared groups did not significantly differ in terms of age, smoking and physical activity.

Patients with abdominal obesity had significantly more frequently metabolic syndrome and all its components excluding hypertension. Obese patients had significantly more frequently increased serum uric acid, and they were significantly more frequently on anti-diabetic therapy (Table 3). There were no significant differences between the compared groups in the frequency of increased blood pressure.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Abdominal obesity (n)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With (n=324)</td>
<td>Without (n=333)</td>
</tr>
<tr>
<td></td>
<td></td>
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</tr>
<tr>
<td>Carotid stenosis ≥70%</td>
<td>261 (80.6%)</td>
<td>283 (85.0%)</td>
</tr>
<tr>
<td>Clinical manifestation of carotid disease</td>
<td></td>
<td></td>
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<tr>
<td>Amaurosis fugax</td>
<td>109 (33.6%)</td>
<td>118 (35.4%)</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>91 (28.1%)</td>
<td>79 (23.7%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>124 (38.3%)</td>
<td>136 (40.8%)</td>
</tr>
</tbody>
</table>

n – number of patients

* According to univariate logistic regression analysis
total cholesterol, LDL cholesterol, high sensitive C-reactive protein and fibrinogen, and in the use of anti-lipid therapy.

Patients with and without abdominal obesity significantly differed in the number of other metabolic syndrome components (p<0.001). Three or four components were present in 51.8% patients with abdominal obesity and in 28.8% of patients without abdominal obesity (Table 4).

Since there were moderate collinearity between the Mets and its components (VIF=2.33), in multivariate logistic regression analysis two models were used. In the Model 1 Mets (but not its components) was included together with other risk factors. In the Model 2, in spite of Mets, its components were included together with other risk factors. According to the results of Model 1, the abdominal obesity was significantly positively associated with female sex, higher Baecke's work index of physical activity, metabolic syndrome and high serum uric acid. According to the results of Model 2, the abdominal obesity was significantly positively associated with female sex, years of school <12, high serum uric acid, increased triglycerides and hyperglycemia (Table 5).

**DISCUSSION**

In the present study, out of 657 participants 324 (49.3%) had abdominal obesity. According to multivariate analyses, abdominal obesity was significantly positively related to female sex, higher Baecke's work index, years of school <12, metabolic syndrome, increased triglycerides, hyperglycemia and high serum uric acid. The number of other metabolic syndrome components (hypertension, hypertriglyceridemia, low level of HDL-C and hyperglycemia) was significantly greater in patients with abdominal obesity than in those without abdominal obesity. Association of abdominal obesity with the Mets and its components (hypertriglyceridemia and hyperglycemia) could have been expected.

There are the literature data supporting the notion that abdominal obesity is predictive of insulin resistance and of the metabolic syndrome [18]. Abdominal obesity influences insulin resistance, a key abnormality associated with metabolic syndrome, as well as alterations in lipids (increased levels of triglycerides and very-low density lipoproteins, and low level of HDL-C), blood pressure, coagulation, fibrinolysis and inflammation, leading to endothelial dysfunction and atherosclerosis [19]. Although there are forms of insulin resistance unrelated to abdominal obesity [20, 21], the most prevalent form of insulin resistance is found among patients with an excess
of abdominal fat [22]. Recent studies that have measured abdominal fat using computed tomography have shown that, out of subjects with abdominal obesity, those with a selective excess of intra-abdominal fat accumulation have the most atherogenic and diabetogenic metabolic profile in comparison with individuals who have selective excess of subcutaneous fat [18, 22, 23].

There are several possible explanations for the observed association between excess visceral fat accumulation and the MetS.

Visceral fat is thought to release fatty acids into the portal circulation, where they may cause insulin resistance in the liver and subsequently in muscles [24, 25].

A parallel hypothesis is that adipose tissue is an endocrine organ that secretes a variety of products that affect atherosclerotic process, such as leptin, interleukin 6, angiotensin II, adiponectin, resistin, tumor necrosis factor-α, inflammatory markers, markers of homeostasis and fibrinolysis and other [26, 27].

Another emerging hypothesis is that excess intra-abdominal fat is a marker of impaired ability of subcutaneous adipose tissue to store excess energy intake, leading to the ectopic storage of fat into nonadipose tissue such as skeletal muscles, liver, heart and even in pancreatic β-cells [28].

Elevated level of uric acid has been shown to be, at least in some studies, an independent predictor of coronary heart disease, stroke and peripheral arterial disease [29-32]. The results of recently published meta-analysis [32] including 16 prospective cohort studies, suggests that hyperuricemia may modestly increase the risks of both stroke incidence and mortality.

There is no agreement about the mechanism through which hyperuricemia increases the risk for cardiovascular disease.

Association of serum uric acid with obesity was reported in several investigations [33, 34]. Abdominal obesity was found to be the main determinant of uric acid variance [35]. Hyperuricemia has been also associated with other MetS components, such as hypertension and dislipidemia (hypertriglyceridemia and decreased values of HDL-C) [36, 37, 38]. A prospective study of 8429 men and 1260 women (20-82 years old) showed that higher serum uric acid is a strong and independent predictor of incident MetS in men and women [39].

Serum uric acid has been related to insulin resistance which in turn is associated with MetS and cardiovascular risk factors. The results of a population-based study which comprised 4536 subjects free from diabetes at baseline and followed during a mean of 10.1 years, suggest that serum uric acid is a strong and independent risk factor for diabetes [40].

There are suggestions that association between uric acid and carotid plaque may be attributable to MetS – dependent and independent mechanisms [41].

In the present study high serum uric acid was related to abdominal obesity independently of MetS, its components, and other atherosclerotic risk factors.

Inverse association between abdominal obesity and education level in the present study, which was independent of sex, was seen in some other populations, but only in women [42, 43]. According to the results of a large cross-sectional study conducted in seven major Latin American cities, Boissonnet et al. [43] concluded that obesity should be considered as a socially-generated disease and an indicator of socioeconomic disadvantages.

Higher Baecke’s work index among our patients with abdominal obesity than in those without abdominal obesity could be explained by the fact that obese patients, because of their lower education, were more frequently blue-collar workers.

The main drawback of the present study is its cross-sectional design which does not make possible to judge causal relationship. Consequently, since all participants had clinical manifestation of carotid atherosclerosis, there was a possibility that analyzed variables might have been changed after the events.

CONCLUSION

In the present study, among patients with symptomatic carotid disease, the abdominal obesity was significantly related to other cardiovascular risk factors, especially metabolic syndrome and its components, and increased serum uric acid.

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REFERENCES


Веза између абдоминалне гојаности и других кардиоваскуларних фактора ризика код особа оболелих од симптоматске каротидне болести – студија пресека

Милош Максимовић1, Христина Влајинац2, Ђорђе Радак3, Јела Маринковић5, Јадранка Максимовић2, Јагода Јорга1

1Институт за хигијену и медицинску екологију, Медицински факултет, Универзитет у Београду, Београд, Србија;
2Институт за епидемиологију, Медицински факултет, Универзитет у Београду, Београд, Србија;
3Институт за кардиоваскуларне болести „Дедиње“, Београд, Србија;
4Медицински факултет, Универзитет у Београду, Београд, Србија;
5Институт за медицинску статистику и информатику, Медицински факултет, Универзитет у Београду, Београд, Србија

КРАТАК САДРЖАЈ
Увод Гојаност, посебно абдоминална, један је од главних фактора ризика за настанак кардиоваскуларних болести.
Циљ рада Циљ рада је био да се утврди веза између абдоминалне гојаности и других фактора ризика за кардиоваскуларне болести.
Методе рада Студијом пресека обухваћено је 657 особа са дијагностикованим каротидном болешћу. Каротидна болест је дијагностикована на основу доплер налаза. Абдоминална гојаност је одређена као обим струка већи од 102 cm код мушкараца и 88 cm код жена.
Резултати Абдоминална гојаност је забележена код 324 испитаника (49,3%). Мултиваријантном анализом је утврђено да је она значајно повезана са женским полом, повећаним Бекеовим (Bvecke) индексом физичке активности на послу, нижком стручном спремом (до 12 година школовања), метаболичким синдромом, повишеном нивоом триглицериде, хипергликемијом и високим нивоом мокраћне кисeline. Пушћење, пијење алкохолних пића, физичка неактивност, повећан ниво укупног холестерола и холестерола мале и велике густине, повишене концентрације С-реактивног протеина и фибриногена и антигликиде и антидијабетичка терапија нису били значајно повезани са абдоминалном гојаношћу.
Закључак Абдоминална гојаност код особа са симптоматском каротидном болешћу значајно је повезана са другим факторима ризика за кардиоваскуларне болести, посебно с метаболичким синдромом, компонентама метаболичког синдрома и високим нивоом мокраћне кисeline.
Кључне речи: абдоминална гојаност; каротидна болест; фактори ризика

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