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### **ORIGINAL PAPER**

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# Correlation of Atherosclerotic Risk Factors with the Size of Abdominal Aortic Aneurysm (AAA)

Clinic for Cardiovascular Surgery, Clinical Center of University of Sarajevo, Sarajevo, Bosnia and Herzegovina

#### Corresponding author:

Nedzad Rustempasic, MD, PhD, Clinic for Cardiovascular Surgery, Clinical Centre of University of Sarajevo, Bolnička 25, phone: +38733298311. E-mail: nrustempasic@yahoo. com. ORCID ID: https:// orcid.org/0000-0002-3980-7683.

# Nedzad Rustempasic, Selma Semic

#### ABSTRACT

Introduction: Abdominal aortic aneurysm represents a local pathological dilatation of the abdominal aorta. It is caused by structural weakness of aortic wall but there are many other risk factors that may positively correlate with incidence of AAA like hypertension, smoking, male gender, older age, family history etc. Aim: The purpose of the study was to evaluate the correlation of atherosclerotic risk factors and the size of aortic aneurysm in patients that were admitted for the surgical treatment at the Clinic for cardiovascular surgery in Sarajevo during period 2016-2019. Methods: The study was designed as a retrospective study with one group of patients that was conducted at the Clinical Center of the University of Sarajevo at the Clinic for Cardiovascular Surgery. It included 150 patients, 126 males and 24 females, all of them with infrarenal localization of AAA. From medical records we have collected relevant anamnestic data (age, gender, positive family history, diabetes mellitus, hypertension, hyperlipidemia, smoking, alcohol consumption and obesity). The size of aneurysm was determined by both ultrasound and CT arteriography. The data are processed in the Statistical Package for Social Sciences Ver. 22.0. The results are tabulated or graphically showed, and level of statistical significance was set at p < 0.05. Results: Total amount of 129 of patients (86%) had hypertension, 57.3% (n=86) of them were smokers, 18.7% (n = 28) were former smokers, and 24% (n = 36) were non-smokers Blood lipid level analysis have shown that 44% (n = 66) of patients were normolipemic, while elevated blood lipid levels were found in 56% (n = 84) of patients. Diabetes mellitus was present in 17.3% (n = 26) of patients, 2.7% (n = 4) of them had an insulin-dependent form, while 14.7% (n = 22) of the analyzed patients had insulin

independent DM. Almost half of total number of patients (46%, n = 69) were obese. 19.3% (n = 29) of patients consumed alcohol while the 80.7% (n = 121) denied alcohol consumption. Ratio of males in comparison to females was 5:1. The average age in males was  $69.79 \pm 8.16$  years and  $72.13 \pm 9.11$  years in females. Significant statistical correlation of AAA size and risk of atherosclerosis factor has not been established. We have found that there is a significant positive correlation between size of aneurysm and risk of rupture (p= 0,000<0,05). **Conclusion:** Although risk factors of atherosclerosis were present, statistically positive correlation was not confirmed between the size of AAA and analyzed risk factors.

Keywords: aneurysm of the abdominal aorta, risk factors of atherosclerosis, statistical correlation.

#### **1. INTRODUCTION**

The exact etiological aspect of aneurysmal degeneration of the abdominal aorta has not been absolutely brought to definite conclusive end. Many factors are involved in it, enzymes like matrix metalloproteinases, genetic influences as well as effect of atherosclerotic lesion on the intima and media. Epidemiological screening studies have demonstrated a higher prevalence of AAA in patients with atherosclerotic risk factors than in the normal population (1-3). The European Society for Vascular Surgery has pointed many risk factors that may positively correlate with incidence of AAA like hypertension, smoking, male gender, older age, family history etc. (4). Female gender, diabetes mellitus, and the black race have had negative correlation to AAA growth (5). Factors that are associated with AAA growth are: chronic obstructive pulmonary disease (COPD), unregulated body weight, impaired fat metabolism, alcohol consumption, and drug use such as antihypertensive, NSAID, corticosteroids and statins (6, 7). Predicting the expansion of AAA and modifying possible risk factors will have important impact on their clinical management.

### **2.AIM**

The purpose of the study was to evaluate the correlation of atherosclerotic risk factors and the size of aortic aneurysm in patients that were admitted for the surgical treatment at the Clinic for cardiovascular surgery in Sarajevo during period 2016-2019.

### **3. METHODS**

This is a clinical retrospective study with one group of patients that was conducted at the Clinical Center of the University of Sarajevo at the Clinic for Cardiovascular Surgery. In this study all analyzed patients were admitted into the hospital during the period 2016-2019 for the surgical repair of AAA. In total, 150 patients were analyzed, 126 males and 24 females. Data have been collected from patient medical history, clinical examination information check list and laboratory results. We have evaluated: age, gender, positive family history for AAA, diabetes mellitus, hypertension, hyperlipidemia, smoking, alcohol consumption and obesity. The size of aneurysm was determined by both ultrasound and CT arteriography. Inclusion criteria were all patients with abdominal aortic aneurysms, their properly completed medical history information related to atherosclerotic risk factors and laboratory findings. Exclusion criteria were incomplete data in the patient history registers and the existence of a suprarenal abdominal aortic aneurysm. The results of the descriptive statistical analysis were presented in terms of statistical tables containing mean values of the aneurysm and the numbers of patients by groups. The inferential statistical analysis was done by testing the differences between mean values of the aneurysm of the independent patient groups. In the case of two independent groups, t-test for independent samples was performed, while in the case of more than two independent groups, one-way ANOVA was performed with Tukey's post-hoc test. The correlations between risk factors and the aneurism were calculated by Spearman coefficient, since there were no conditions for the calculation of pointbiserial correlation (the pre-conditions for its application were tested by Shapiro-Wilk and Kolmogorov-Smirnov test).

## 4. RESULTS

A total of 150 patients diagnosed with AAA were included in study, 84% (n=126) males and 16% (n=24) females. The average age of patients was 69,17  $\pm$  8,34. The youngest patient was 49 and the oldest 90. The average age of female was 72,13  $\pm$  9,11 and the average age of males was 69,79  $\pm$  8,16. Ratio of males in comparison to females was 5:1.

An analysis of risk factors in the total sample (n=150) we have found the following results: 86% of patients (n=129) had hypertension and 57.3% (n=86) of them were smokers, 18.7% (n = 28) were former smokers, and 24% (n = 36) were non-smokers Blood lipid level analysis have shown that 44%

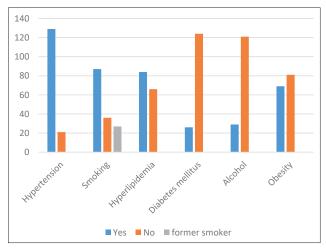


Figure 1. Risk factors distribution

| Average size of aneurysm | 6,232 ±<br>1,3058 |        |            |
|--------------------------|-------------------|--------|------------|
| Aneurysm classification  | Size              | Number | Percentage |
| Small aneurysm           | >3 cm-5 cm        | 22     | 14,7       |
| Medium-sized aneurysm    | >5 cm-<7 cm       | 101    | 67,3       |
| Giant aneurysm           | ≽7 cm             | 27     | 18,0       |

Table 1. Prevalence of different types of aneurysms according to their size

| Risk factors   | Modalities               | Size of aneurysm |                    |       |
|----------------|--------------------------|------------------|--------------------|-------|
|                |                          | Mean             | Number of patients | р     |
| Gender         | Male                     | 6,2              | 126                | 0,913 |
|                | Female                   | 6,2              | 24                 |       |
| Alcohol        | Use                      | 6,1              | 29                 | 0,551 |
|                | Not                      | 6,3              | 121                |       |
| Obesity        | Yes                      | 6,4              | 69                 | 0,146 |
|                | No                       | 6,1              | 81                 |       |
| Family history | No relatives             | 6,0              | 48                 | 0,335 |
|                | One relative             | 6,3              | 79                 |       |
|                | More rela-<br>tives      | 6,4              | 23                 |       |
| DM             | No                       | 6,2              | 124                | 0,750 |
|                | Insulin<br>dependent     | 5,8              | 4                  |       |
|                | Insulin inde-<br>pendent | 6,3              | 22                 |       |
| HTA            | No                       | 6,1              | 21                 | 0,494 |
|                | Controlled               | 6,3              | 109                |       |
|                | Poorly con-<br>trolled   | 6,0              | 19                 |       |
| Hyperlipidemia | Normal                   | 6,0              | 66                 | 0,080 |
|                | High                     | 6,4              | 84                 |       |
| COPD           | Yes                      | 6,5              | 25                 | 0,371 |
|                | No                       | 6,2              | 125                |       |
| Smoking        | Yes                      | 6,1              | 87                 | 0,479 |
|                | No                       | 6,2              | 36                 |       |

Table 2. Comparison of subgroups of risk factors to the size (mean) of evaluated AAA

| Risk factor         | Gender                     | Diabetes<br>Mellitus | HTA    | Hyperli-<br>pidaemia | COPD  | Smoking | Family<br>history | Alcohol | Obesity | Number<br>of RF |       |
|---------------------|----------------------------|----------------------|--------|----------------------|-------|---------|-------------------|---------|---------|-----------------|-------|
| SIZE OF<br>ANEURYSM | Correlation<br>Coefficient | 0,022                | -0,014 | 0,022                | 0,093 | 0,074   | 0,064             | 0,115   | -0,021  | 0,118           | 0,126 |
|                     | Sig.<br>(2-tailed)         | 0,790                | 0,868  | 0,791                | 0,256 | 0,369   | 0,440             | 0,160   | 0,794   | 0,151           | 0,125 |
|                     | N                          | 150                  | 150    | 150                  | 150   | 150     | 150               | 150     | 150     | 150             | 150   |

Table 3. Correlation of risk factors with aneurysm size

(n = 66) of patients were normolipemic, while elevated blood lipid levels were found in 56% (n = 84) of patients. Diabetes mellitus was present in 17.3% (n = 26) of patients, 2.7% (n = 4) of them had an insulin-dependent form, while 14.7% (n = 22) of the analyzed patients had insulin independent DM. Almost half of total number of patients (46%, n = 69) were obese. 19.3% (n = 29) of patients consumed alcohol while the 80.7% (n = 121) denied alcohol consumption (Figure 1).

Aneurysm size was measured in all 150 subjects. Average aneurysm size was  $6,232 \pm 1,3058$  cm., with the size ranging from 3.0 cm to 10.2 cm. There are three types of aneurysms sorted by size (small, medium sized and giant aneurysm). In 14,7% of patients (n = 22) we have observed small size aneurysms, medium-sized aneurysms were found in 67,3% (n = 101) of patients. Giant aneurysms (greater than 7 cm) were diagnosed in 18,0% (n = 27) of patients (Table 1).

Individual comparison of subgroups of tested risk factors with the size of aneurysm have not shown any statistical significance (Table 2).

We have not established statistically significant correlation between the number of present risk factors (RF) and the size of aneurysm (p 0,496>0,05) (Table 4).

| Number of RF | Size of aneurysm | Number of patients |
|--------------|------------------|--------------------|
| 1            | 5,5              | 2                  |
| 2            | 6,0              | 9                  |
| 3            | 6,2              | 31                 |
| 4            | 5,9              | 34                 |
| 5            | 6,6              | 27                 |
| 6            | 6,5              | 36                 |
| 7            | 6,2              | 10                 |
| 8            | 5,8              | 1                  |
| Total        | 6,2              | 150                |
| P =0,496     |                  |                    |

Table 4. Size of aneurysm in relation to the number of risk factors

There was statistically significant correlation between size of aneurysm and the risk of rupture (p=0,000<0,05). (Table 5)

#### **5. DISCUSSION**

Hypertension in our study was present in 86% (n = 129) of patients. These data have shown high prevalence of hypertension in AAA patients. Some studies indicate that high blood pressure and diagnosed hypertension are a significant risk factor in the development of AAA while Lee and Blanchard along with their associates pointed out that increased diastolic pressure had no significant association with the development of AAA (8, 9). Singh has noted in his research that high systolic pressure is a risk

| Variable  |  | Mean | Number of patients | Р     |
|---|--|------|--------------------|-------|
| Aneurysm<br>classifica-<br>tion ac-<br>cording to<br>the size | Small aneurysm 3 cm<br>do ≤5 cm        | 4,4  | 22                 | 0,000 |
|   | Medium-sized aneu-<br>rysm >5 do ≤7 cm | 6,1  | 101                |       |
|   | Giant aneurysm >7 cm                   | 8,3  | 27                 |       |
| Aneurysm<br>Risk<br>Rupture                                   | 0% Aneurysm ≤4 cm                      | 3,7  | 5                  | 0,000 |
|   | 0,5–5%–Aneurysm 4<br>do ≤5 cm          | 4,6  | 17                 |       |
|   | 3-15%–Aneurysm 5<br>do ≤6 cm           | 5,7  | 56                 |       |
|   | 10-20%-Aneurysm 6<br>do ≤7 cm          | 6,6  | 45                 |       |
|   | 20 do 40%-Aneurysm<br>7 do ≤8 cm       | 7,7  | 17                 |       |
|   | 30 do 50%–Aneurysm<br>>8 cm            | 9,4  | 10                 |       |
|   |  |      |                    |       |

Table 5. Aneurysm risk rupture in relation to the size of aneurysm

factor only for women (7). The association of aneurysm cases with hypertension was observed in our study but its correlation with the size of aneurysm was not statistically significant (p = 0.791). In our study more than half of the patients (57.3%, n = 86) were smokers, while 24% (n = 36) of patients were non-smokers and 18.7% (n = 28) of patients were former smokers. According to the European Society of Vascular Surgery, smoking is the highest risk factor for the development and progression of an abdominal aortic aneurysm (4). Most studies have proved significant association between smoking and AAA. We have not established their statistically significant correlation (p = 0.440). 56% of our patients (n = 84) had hyperlipidemia. There was no significant correlation of hyperlipidemia with different sizes of analyzed abdominal aneurysms (p=0,256). These results are consistent with Blanchard's research, where he has observed that hypercholesterolemia, LDL cholesterol values, HDL cholesterol levels are not associated with AAA (9). Thornwall noted in his study that high blood pressure and hypercholesterolemia correlated positively with the development of AAA (10). Obesity in our patients was present in 46% (n = 69) of cases and there was no significant correlation between aneurysm size and obesity, p = 0.151. Our data correlated with the results published in Cronin and Stackelberg study, where no clear association was established between obesity and AAA (11, 12). Exercise has not been shown to slow AAA growth. There is an initiative by some authors towards need to do some research on whether obesity is a risk factor for AAA growth at all (4). We did not find a significant positive association between alcohol consumption and AAA growth. Among our patients,

19.3% of them (n = 29) consumed alcohol, which is in agreement with data from a study conducted by Forsdahl et al. (13). A negative association between alcohol and AAA was also reported by Tornwall et al. (10). Patients with diabetes mellitus have slower growth in AAA than patients without diabetes mellitus, which has been linked to the use of metformin in patients with type II DM. Rango et al., have analyzed over 389 reports related to diabetes mellitus and AAA and they concluded that patients with DM had a lower prevalence of AAA.

Based on the classification of the aneurysm by size, 15% of our patients had small sized aneurysms (n = 22), majority of analyzed patients belong to medium size group-67% of patients (n = 101), and 18% (n = 27) of patients had giant sized aneurysm. According to the aneurysm size data, we calculated the risk of rupture in our subjects. Out of total number of patients (n = 150), 37.3% (n = 56) had aneurysm size ranging from 5 to 6 cm and their risk of rupture ranged from 3 to 15% / year. 30% of patients (n = 45) had a risk of rupture ranging from 10 to 20% / year. 11.3% of patients (n = 17) had a risk of rupture from 0.5 to 5% / year and 18% (n = 27) of patients had a rupture risk greater than 20% / year. We have established statistically significant risk of rupture in our group of patients according to size of aneurysm (p=0.000 < 0.05). Similar data are found in autopsy studies, which confirms the significant incidence of aneurysm ruptures with an average diameter around 6 cm (14).

# **6. CONCLUSION**

No statistically relevant correlation between factors of atherosclerosis and the size of abdominal aneurysm was established in our study while at the same time we have established statistically significant correlation between size of aneurysm and risk of aneurysm rupture. This study was not designed to evaluate the cause of aneurysm appearance but just the correlation of atherosclerotic risk factors with aneurysm size. Therefore, it is important to continue to implement regular monitoring of growth of aneurysm for all patients irrespective of their age, gender, smoking habits, presence of hypertension or diabetes mellitus since there is clearly established genetic and enzyme degradation background of aneurysm origin.

- Author's contribution: N.R. and S.S. gave a substantial contribution to the conception and design of the work and in the acquisition, analysis and interpretation of data for the work. NR had a part in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Conflicts of interest: There are no conflicts of interest.
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