

THE CARDIOVASCULAR RISK FACTORS AND THEIR EFFECT ON THE THORACIC AORTIC ANEURYSM SIZE - A PILOT STUDY

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All the authors contributed significantly to the research that resulted in the submitted manuscript.

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ABSTRACT

Objective: The aim of this study was to determine the impact of age, gender, systemic arterial hypertension, diabetes mellitus, dyslipidemia and smoking on the thoracic aortic aneurysm size.

Methodology: This pilot study was conducted at Department of Cardiovascular AHEPA University Hospital, Thessaloniki, Greece from May 2009 to May 2011. Aneurismal size was measured in 26 consecutive patients with thoracic aortic aneurysm. They underwent a series of three computer tomography images.

Results: Older patients and smokers tended to have elevated mean aneurysm diameter (4.88 ± 0.97 vs. 4.69 ± 0.74 cm, 5.08 ± 0.16 vs. 4.50 ± 0.10 cm, $p=0.067$, $p=0.0023$ respectively). Dyslipidemic patients treated with statins tended to have smaller mean aneurysm dimensions (4.53 ± 0.11 vs. 4.84 ± 0.13 cm respectively, $p=0.074$).

Diabetic patients tended to have smaller mean aneurysm dimensions (4.44 ± 0.17 vs. 4.74 ± 0.10 cm, $p=0.139$). Well controlled arterial hypertension had no effect on the mean aneurysm size (4.68 ± 0.84 vs. 4.58 ± 0.10 cm, $p=0.737$).

Conclusion: Smoking, older age had a positive association with the thoracic aortic aneurysm size, dyslipidemic patients treated with statins tended to have smaller mean aneurysm size. Diabetic patients tended to have smaller mean aneurysm size.

Key Words: Thoracic Aortic Aneurysm, Cardiovascular Risk Factors

INTRODUCTION

The major risk factors for aortic aneurysm include: age, male gender, smoking, systemic arterial hypertension and atherosclerotic disease.¹⁻³ The atherosclerotic profiles are significantly different between patients with thoracic aortic aneurysm (TAA) and patients with abdominal aortic aneurysm (AAA) with a higher incidence of hypertension in the patients with TAA.⁴ Atherosclerosis and smoking history are associated with accelerated growth of the thoracic aortic aneurysms.⁵ Moreover the protective role of the diabetes on the development of AAA had been described.⁶ Our study aimed to examine the incidence and impact of the common cardiovascular risk factors of age, gender, systemic arterial hypertension, diabetes mellitus, dyslipidemia and smoking that might influence the thoracic aortic aneurysm size.

METHODOLOGY

This pilot study was conducted at Department of Cardiovascular AHEPA University Hospital, Thessaloniki, Greece from May 2009 to May 2011. Twenty six consecutive patients who presented to the outpatient clinic of the Cardiovascular Department of the AHEPA University hospital, Thessaloniki, Greece, with uncomplicated thoracic aortic aneurysms and diameter above 4 cm were included in this study. Eighteen patients (69.2%) were aware of the presence of the aneurysm and for the remainder eight patients (30.8%), the presence of the aneurysm was an incidental finding by the cardiologists. Patients with ruptured/symptomatic thoracic aortic aneurysms were excluded from the study.

The patients underwent a series of three computer tomography (CT) images of the thoracic aorta. The scans were performed at six and 12 months after the first one.

Computer assisted tomography was used to visualize the aorta and to determine the maximal aneurysm diameter. The CT scans that used were the Tomoscan SR 700 (Philips) and the Somatom Emotion 16 (Siemens). The field of view was 370 cm. Firstly without contrast material sequential cuts of 10 cm each were done from the lung apices to the lung bases for the anatomic evaluation of the aorta and the presence of any atherosclerotic plaque. Afterwards with the infusion of 120 ml of any commercially available non-ionic contrast material at a rate 3.2 ml/sec and using the spiral technique, cuts of 5mm were done after the initiation of the infusion of the contrast material in two planes. The first plane is cephalad-caudal from the level of the aortic arch to the lung bases and the second plane is caudo-cephalad from the lung bases to the lung apices. Finally the measurements of the maximal aortic diameter at any level of the thoracic aorta were taken. The same protocol of measurement was chosen to measure the aneurysm size in the follow-up.

One way ANOVA was used to assess the independent effect of gender, age, smoking, hypertension, dyslipidemia and diabetes mellitus on aneurysm size. For the statistical analysis the software of JMP (Version 4, SAS Institute Inc., Cary, NC, USA) were used. Student's t was used to calculate p value. The data are given as mean value \pm SD (standard deviation). P value of < 0.05 was taken as statistically significant.

RESULTS

Twenty-one patients (80.8%) were male and five patients (19.2%) were female. Mean age was 63.57 ± 11.28 years (45 to 80). The patients were categorized according to their age in three groups. The first group was from age 45 to 55 years old, the second group was from age 56 to 68 years old and the last group was from 69 to 80 years old. Twenty-two patients had involvement of the ascending aorta and four patients involvement of the descending aorta. The cause of aneurysms was atherosclerotic disease in majority. Two of the patients with involvement of the descending aorta had also aneurysmal involvement of the abdominal aorta. The first patient underwent replacement of the abdominal aorta and the second one underwent endovascular stent insertion. Four patients had symptomatic concomitant coronary artery disease with one patient treated with coronary artery bypass graft (CABG) and the other three patients with percutaneous coronary intervention (PCI). Finally, the two patients with a thoracoabdominal aneurysm had also symptomatic coronary artery disease treated with PCI. The baseline characteristics of the patients are shown in Table 1.

The mean maximal aneurysm dimension was 4.66 ± 0.77 cm. The range of the thoracic aortic aneurysms were 4.1-7.8 cm. The mean aneurysm dimensions of each the three measurements of all the patients were 4.4 ± 0.77 cm, 4.4 ± 0.77 cm, and 4.4 ± 0.8 cm respectively with no significant statistical difference between the three measurements ($p = \text{NS}$).

Concerning the prevalence of the various cardiovascular risk factors, 21 patients (80.8%) suffered from arterial hypertension, seven patients (26.9%) had a history of diabetes mellitus, eight patients (30.8%) had a history of smoking and 11 patients (65.4%) had a history of dyslipidemia.

From the risk factors for cardiovascular disease only smoking, age above 69 years old and dyslipidemia showed association with the aneurysm size. The aneurysm diameter (mean 95%) of the patients at the age group above 69 years old and those who are smokers tended to be elevated compared with the other patients. Patients with age above 69 years old had mean diameter 4.88 ± 0.97 cm versus 4.51 ± 0.74 cm for younger patients ($p = 0.067$).

Table 1: Baseline Characteristics

Variables	Frequency (%)
Mean Age (Years)	63.57±11.28
Age Range (Years)	45-80
Female	5 (19.2%)
Male	21 (80.8%)
Medical History	
Hypertension	21 (80.8%)
Diabetes Mellitus	7 (26.9%)
Smoking	8 (30.8%)
Dyslipidemia	17 (65.4%)
CHF	2 (7.7%)
AF	1 (3.8%)
Stroke	1 (3.8%)
Liver disease	1 (3.8%)
Crohn's Disease	1 (3.8%)
Location of the aneurysm	
Ascending Aorta	22 (84.6%)
Descending Aorta	4 (15.4%)
Management	
CABG	1 (3.8%)
PTCA	3 (11.5%)
AVR	4 (15.4%)
Replacement Asc. Aorta	4 (15.4%)
Endovascular Stent in AAA	1 (3.8%)
Replacement of AAA	1 (3.8%)
Medications	
Statins	15 (57.7%)
β-blockers	18 (69.2%)
Calcium Channels Blockers	6 (26.1%)
ACE Inhibitor/ARB	19 (73.1%)

CHF=Congested Heart Failure,
 AF=Atrial Fibrillation,
 CABG=Coronary Artery Bypass Grafting,
 PTCA=Percutaneous Tranluminal Coronary Angioplasty,
 AVR=Aortic Valve Replacement,
 AAA=Aneurysm of Abdominal Aorta,
 ACE Inhibitor/ARB=Angiotensin Converting Enzyme,
 Inhibitor/Angiotensin Receptor Blocker

Moreover smokers had larger mean aneurysm dimensions ($p=0.0023$) than non-smokers (5.08 ± 0.16 cm vs. 4.5 ± 0.10 cm for non-smokers).

The mean aneurysm diameter of the dyslipidemic patients tended to be smaller, 4.53 ± 0.11 cm for dyslipidemic patients and 4.84 ± 0.13 cm for non-dyslipidemic patients ($p=0.0704$).

The association between hypertension, diabetes mellitus and sex with the aneurismal size is non-significant ($p=0.737$, $p=0.139$ and $p=0.461$ respectively).

Firstly, concerning the hypertension the mean aneurysm dimension of the hypertensive patients with well controlled disease was 4.68 ± 0.84 cm. On the other hand the mean aneurysm dimension of the non-hypertensive patients was 4.58 ± 0.36 cm.

Secondly, concerning the diabetes mellitus, diabetic patients had smaller mean aneurysm diameter 4.44 ± 0.17 cm, comparing with the non-diabetic patients 4.74 ± 0.10 cm, although this difference in this study was statistically non-significant.

Finally, the gender of the patients had no effect on the aortic aneurysm dimension. Male patients had mean aneurysm dimension of 4.69 ± 0.82 cm, whereas female patients had mean aneurysm dimension of 4.52 ± 0.44 cm.

Table 2 shows the association of the risk factors of hypertension, dyslipidemia, diabetes mellitus, smoking and the patients medical history with the aneurismal size. Table 3 shows patients characteristics, medical therapy and follow up CT measurement of each individual patient.

DISCUSSION

In our study we observe that the gender of the patient has no association with the aneurismal size. Moreover patients older than 69 years old had larger thoracic aortic aneurysm dimensions comparing with younger than 69 years old patients. This may have a multi factorial aetiology due to the impact of the various risk factors of atherosclerosis that affect the aortic wall in combination with the annual growth

Table 2: Association of the Various Risk Factors with the Aneurismal Size

Variables	Mean Aortic Diameter ± SD		P-value
	Presence	Non-Presence	
Hypertension	4.68 ± 0.84 cm	4.58 ± 0.36 cm	0.737
Smoking	5.08 ± 0.16 cm	4.50 ± 0.10 cm	0.0023
Dyslipidemia	4.53 ± 0.11 cm	4.84 ± 0.13 cm	0.0704
Diabetes Mellitus	4.44 ± 0.17 cm	4.74 ± 0.10 cm	0.139

Table 3: Patients Characteristics, Medical Therapy and CT Measurements in Follow up

Patient S.No	Age	Gender	Risk Factors	Medical Therapy	Location	1 ST CT/cm	2 nd CT/cm	3 RD CT/cm
Patient 1	66	F	HTN	ACE inh/ARB, β -blocker, statin	AA	4.1	4.2	4.2
Patient 2	63	M	HTN,DM	β -blocker, CCB	AA	4	4	4
Patient 3	75	M	DM,D	CCB,statin	AA	4.3	4.3	4.4
Patient 4	64	M	HTN,S,D	ACE, β -blocker, statin	AA	5.4	5.4	5.4
Patient 5	59	M	DM,D	statin	AA	5	5	5
Patient 6	50	M	HTN	β -blocker	AA	6	6	
Patient 7	80	M	HTN,DM,D	ACE inh/ARB, β -blocker, CCB, statin	AA	5	5	5
Patient 8	70	M	HTN,D	ACE inh/ARB, statin	AA	4.4	4.4	4.4
Patient 9	74	F	HTN,DM,D	ACE inh/ARB, β -blocker, statin	AA	4	4	4
Patient 10	46	M	HTN	ACE inh/ARB	AA	4.4	4.4	4.4
Patient 11	46	M	D	β -blocker,statin	AA	4.4	4.4	4.4
Patient 12	70	F	HTN,D	ACE inh/ARB, β -blocker	AA	4.4	4.4	
Patient 13	74	M	HTN,S	ACE inh/ARB, β -blocker, CCB	DA	5	5	5
Patient 14	59	M	HTN,D	ACE inh/ARB, β -blocker, statin	AA	4.1	4.1	4.1
Patient 15	63	M	HTN,S,D	ACE inh/ARB, β -blocker,statin	DA	4	4	4
Patient 16	77	M	HTN,S	ACE inh/ARB	DA	7.5	7.5	7.8
Patient 17	73	M	HTN	ACE inh/ARB, β -blocker	AA	4.8	4.8	4.8
Patient 18	47	M			AA	4.2	4.2	4.2
Patient 19	60	M	HTN,S	ACE inh/ARB, β -blocker, CCB	DA	4.5	4.5	4.5
Patient 20	72	F	HTN,D	ACE inh/ARB, β -blocker,statin	AA	5	5	5
Patient 21	78	M			AA	5	5	5
Patient 22	54	M	HTN,DM,D	ACE inh/ARB, β -blocker, statin	AA	4.7	4.7	4.7
Patient 23	53	F	HTN,S,D	ACE inh/ARB, β -blocker, statin	AA	5	5	5
Patient 24	78	M	HTN,D	ACE inh/ARB, β -blocker, statin	AA	4	4	4
Patient 25	57	M	HTN	ACE inh/ARB, β -blocker	AA	4	4	4
Patient 26	45	M	HTN,DM,S,D	ACE inh/ARB, β -blocker, statin	AA	4.1	4.1	4.1

M= Male, F=Female, HTN=Hypertension, DM=Diabetes Mellitus, D=Dyslipidemia, S=Smoking, ACE inh/ARB=Angiotensin Converting Enzyme Inhibitor/Angiotensin Receptor Blocker, CCB=Calcium Channel Blocker, AA=Ascending Aorta, DA=Descending Aorta

rate of aneurysms (ascending aorta 0.1 mm/year, descending aorta 0.3 mm/year) which might be also accelerated by the effect of the various risk factors.^{5,7}

Also smoking history showed a consistently positive effect on aneurysm dimension with this group of patients having larger thoracic aortic dimensions than the non-smoker's group. This is in accordance with other studies and may reflect the effect of smoking on connective tissue which was previously shown in abdominal aortic aneurysms.^{8,9} These data support the need for smoking cessation advice in such patients.

In our study the presence of hypertensive history was not associated with the aortic aneurysm dimension. Although these data were consistent with previous reports they should be considered cautiously, as all hypertensive patients were undergoing treatment with b-blockers and other hypertensive drugs during this study and therefore adequate blood pressure control could nullify any positive expansion effect of this variable.¹⁰

Dyslipidemic patients had the tendency to have smaller aneurysm dimensions. It may be attributed to the use of statins by these patients. It appears that the statin exposure slows down the aneurysm expansion and affects the aneurysm progression. Recently study by Jovin et al, showed that the intake of statins was associated with an improvement in long-term outcomes in this cohort of patients with thoracic aortic aneurysm and this was driven mainly by a reduction in aneurysm repair.¹¹ Also the aneurysm growth rate difference was significant over time (0.09 vs. 0.12 cm/year in patients on and off statins). It is likely that the statins' protective effects were pleiotropic. They have anti-inflammatory effects, and they also address some of the abnormalities that are believed to be involved in the genesis of aneurysms.

In a recently published study by McLoughlin et al, it was shown that the use of pravastatin in a mouse model of Marfan syndrome reduced aortic dilatation and elastin loss in a similar fashion like losartan.^{12,13}

In our study the presence of diabetes mellitus was not associated with the aneurysm size. Diabetic patients tended to have smaller aneurysm dimensions than non-diabetic patients. This correlates with recently published evidence. The protective effect of diabetes mellitus in the development of abdominal aortic aneurysms is well established and the expansion rate of the aneurysm is slower.⁶

Concerning the thoracic aortic aneurysms Prahash et al, in a nationwide case-control study showed that diabetes is associated with a decreased rate of hospitalization due to thoracic aortic aneurysms and dissections in proportion to the severity of diabetic complications.¹⁴ With enhanced glycation as in diabetes mellitus more glycosylated monomeric

collagen may be formed, with effects on MMP (metalloproteinase) secretion and marked reduction of MMP-9, MMP-2, and interleukin-6 secretion by activated monocytes, thereby inducing cross-links likely to increase matrix and aortic wall stiffness.¹⁵

Also the extend of aortic aneurysm was examined in this analysis. From the literature is known that patients with abdominal aortic aneurysms have high frequency of thoracic aneurysm. This was studied by Larsson et al, and Chaer et al.^{16,17} They found that thoracic aortic aneurysms are relatively common in patients with abdominal aortic aneurysms and more than one fourth of patients with abdominal aortic aneurysm have a concomitant thoracic aortic aneurysm and women are particularly affected. The majority of the patients suffered from aneurysm of the descending aorta or had both ascending and descending aortic aneurysms.

Another interesting study by Achneck et al, shows that patients with ascending thoracic aneurysms (annuloaortic ectasia or type A of dissection) are associated with decreased systemic atherosclerosis.¹⁸ These findings are consistent with related studies in the literature as is also seen in our study. A lower incidence of coronary disease was found among patients with thoracic aortic dilatation compared to those with the same pathology in the abdominal aorta.^{19,20} Finally, the two patients of our study group with a thoracoabdominal aneurysm had also symptomatic coronary artery disease which was treated with a percutaneous coronary intervention. This association of thoracoabdominal aneurysms with the coronary artery disease was referred also by other authors and this resulted in increased postoperative morbidity and mortality.^{20,21}

STUDY LIMITATIONS

The limitation of the study is the small number of participants and short follow-up time in order to establish any association between the various cardiovascular risk factors and the aneurysm growth rate. However this study is one of the many others that were done concerning this question and all of them shows in which direction future larger studies with longer follow-up should be done in order definitively to establish the association between the thoracic aneurysm size and the aneurysm growth rate and the various cardiovascular risk factors.

CONCLUSION

In conclusion in our study it is shown that smoking, older age and dyslipidemia have an association with the thoracic aortic aneurysm size with the dyslipidemic patients having smaller aneurysm dimensions. On the other hand the association between hypertension, diabetes mellitus and gender with the aneurysmal size is non-significant.

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