Original Article

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Relationship of homocysteine level with abdominal aortic aneurysm and coronary artery disease

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ABSTRACT

Objectives: The aim of the present study was to investigate the relationship of homocysteine levels with major atherosclerotic diseases in patients with coronary artery disease undergoing coronary artery bypass grafting (CABG) and in patients with infrarenal abdominal aortic aneurysms (AAAs).

Patients and methods: This prospective, case-control study included a total of 55 patients (35 males, 20 females; median age 64 years; range, 42 to 83 years) undergoing CABG and patients with infrarenal AAAs between January 2015 and June 2015. The infrarenal AAA group (n=15) consisted of the patients having an anteroposterior diameter of ≥50 mm and the CABG group (n=20) consisted of the patients who underwent CABG during the study period. The patients without any known AAA were assigned to the control group (n=20). Homocysteine, low-density lipoprotein cholesterol (LDL-c), and triglyceride levels were analyzed in all groups.

Results: Homocysteine levels were significantly higher in the AAA group than both in the CABG group (p=0.039) and in the control group (p=0.011). No significant differences in the homocysteine levels (p=0.072) were found both between the patients with low and high LDL-c levels (p=0.345) and between the patients with low and high triglyceride levels.

Conclusion: Our study results suggest that homocysteine level is directly associated with AAAs and may be useful to identify patients with an AAA.

Keywords: Abdominal aortic aneurysm, coronary artery disease, homocysteine.

The most common aortic pathology is the abdominal aortic aneurysm (AAA) which is defined as an enlargement of the transverse diameter of the abdominal aorta more than 50%.[1,2] Stenosis and occlusion of one or more coronary arteries, which can lead to different clinical manifestations, such as acute myocardial infarction, unstable angina, and stable angina, is referred to as coronary artery disease (CAD). Coronary artery disease and AAA are two major diseases caused by atherosclerosis.[3]

The role of homocysteine in the development of atherosclerosis has not been clearly elucidated yet; however, the relationship between atherosclerosis and hyperhomocysteinemia has been reported in various observational studies in the literature.[4] In the present study, therefore, we aimed to investigate the relationship of homocysteine levels with major atherosclerotic diseases in CAD patients undergoing coronary artery bypass grafting (CABG) and in patients with infrarenal AAAs.

PATIENTS AND METHODS

This prospective, case-control study included a total of 55 patients (35 males, 20 females; median age 64 years; range, 42 to 83 years) undergoing CABG and patients with infrarenal AAAs at the Department of Cardiovascular Surgery of Dokuz Eylul University, Faculty of Medicine, Izmir, Turkey between January 2015 and June 2015. Patient under 18 years old, having CAD accompanied with valve

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disease, having an AAA accompanied with CAD, and those having end-stage renal failure were excluded. Ruptured AAA and emergent CABG cases were also excluded. A written informed consent was obtained from each patient. The study protocol was approved by the local Ethics Committee of Dokuz Eylul University, Faculty of Medicine (Date: 25/12/2014, No. 1801). The study was conducted in accordance with the principles of Declaration of Helsinki.

The infrarenal AAA group consisted of the patients having fusiform type aneurysms with an anteroposterior diameter of ≥50 mm. All aneurysms were detected by contrast-enhanced computed tomography (CT). The CAD group consisted of the patients who underwent isolated CABG during the study period. The patients in the control group were randomly selected from the hospitalized patients in other clinics (geriatric clinic and dermatology clinic) for other minor medical conditions. Abdominal ultrasonography was performed to the control group to exclude AAAs.

In all study groups, homocysteine, low-density lipoprotein cholesterol (LDL-c), and triglyceride levels were analyzed. Triglyceride and LDL-c levels were measured using the kits (Beckman Coulter, Fullerton, CA, USA) in the Olympus AU 5800 (Olympus Co., Tokyo, Japan) analyzer. Venous blood samples (about 4 mL) of each participant were collected using vacutainer tubes containing ethylenediaminetetraacetic acid (Becton-Dickinson, San Jose, CA, USA) and were centrifuged at 3,000 rpm for five min. The plasma samples were kept at -80°C prior to the analysis of homocysteine levels. Homocysteine levels were assessed quantitatively by fluorescence polarization immunoassay (Agilent 1100 HPLC, Agilent Technologies, Waldbronn, Germany). The homocysteine levels >15 μmol/L were accepted as hyperhomocysteinemia.

Statistical analysis

The sample was calculated with this sample size, there is about 85% likelihood that study would yield statistical results and allow us to conclude that the percentage of subjects (Power and Precision V4). Statistical analysis was performed using the PASW version 17.0 software (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed in mean ± standard deviation (SD) and median (min-max). In multiple independent group comparisons, one-way analysis of variance (ANOVA) test was used for normally distributed numerical variables. In comparison of two independent groups, the Mann-Whitney U test was used for non-normally distributed numerical variables. A p value of <0.05 was considered statistically significant.

RESULTS

Of the patients, 15 were in the AAA group (median age, 77.6 years; range, 54 to 72 years), 20 were in the CABG group (median age, 61.8 years; range, 42 to 72 years), and 20 were in the control group (median age, 59 years; range, 42 to 79 years), (Tables 1 and 2).

Table 1. Demographic and clinical characteristics of patient groups

	Abdominal aortic aneurysm (n=15)	Coronary artery disease (n=20)	Control (n=20)	
	n	n	n	*p*
Gender				
Male	13	16	6	0.001
Hyperlipidemia	7	8	15	NS
Hypertension	9	10	17	NS
Chronic obstructive pulmonary disease	10	12	10	NS
History of smoking	12	17	8	0.005
Diabetes mellitus	10	12	16	NS

NS: Non-significant (p<0.05).

Table 2. Comparison of study groups in term of body mass index, age, and aneurysm diameter

	Abdominal aortic aneurysm	Coronary artery disease	Control	
	Mean±SD	Mean±SD	Mean±SD	*p*
Age (year)	65.6±6.7	64.6±9.9	63.3±12.1	NS
Body mass index (kg/m^2)	26.1±3.1	26.5±3.9	29.8±4.4	0.01
Aneurysm diameter (mm)	61.0±15.6			

SD: Standard deviation; NS: Non-significant (p<0.05).

Table 3. Comparison of the study groups in terms of homocysteine levels

	Abdominal aortic aneurysm (n=15)	Coronary artery disease (n=20)	Control (n=20)			
	Mean±SD	Mean±SD	Mean±SD	p^1	p^2	p^3
Homocysteine levels (µmol/L)	16.9±7.0	12.9±6.9	12.9±4.7	0.039	0.011	0.808

SD: Standard deviation.
p^1 for the comparison of the abdominal aortic aneurysm group with the coronary artery bypass grafting group.
p^2 for the comparison of the abdominal aortic aneurysm group with the control group.
p^3 for the comparison of the coronary artery bypass grafting group with the control group.

Table 4. Comparison of the patients according to cardiovascular risk factors regarding homocysteine levels

		Homocysteine levels (µmol/L)			
Groups	n	Mean±SD	Median	Min-Max	*p*
LDL-c <100	20	15.8±8.7	13.25	2.00-36.70	0.345
LDL-c ≥100	35	13.0±4.4	12.70	3.95-24.30	
TG <150	32	13.1±7.0	11.95	2.00-36.70	0.072
TG ≥150	23	15.2±5.2	14.30	6.70-26.30	

SD: Standard deviation; Min: Minimum; Max: Maximum; LDL-c: Low-density lipoprotein cholesterol; TG: Triglyceride.

A comparison of the study groups in terms of homocysteine levels is presented in Table 3. Homocysteine levels were significantly higher in the AAA group than both in the CAD group (p=0.039) and in the control group (p=0.011); however, there was no significant difference in the homocysteine levels between the CAD and control groups (p=0.808).

When the patients were further divided according to their LDL-c and triglyceride levels, which are well-established as the major cardiovascular risk factors, no significant differences in the homocysteine levels (p=0.072) were found both between the patients with low and high LDL-c levels (p=0.345) and between the patients with low and high triglyceride levels (Table 4).

DISCUSSION

In the present study, we investigated the relationship of homocysteine levels with major atherosclerotic diseases in CAD patients undergoing CABG and in patients with infrarenal AAAs. We found that homocysteine levels were higher in AAA patients, compared to both CAD patients and controls. However, homocysteine level did not significantly differ according to LDL-c and triglyceride levels of the patients. In the literature, the importance of homocysteine was shown in two major studies by Wilcken and Wilcken[5] in 1976 in patients with CAD and Brattstrom et al.[6] in 1984 in patients with cerebrovascular disease. In another study by Clarke et al.,[7] moderate hyperhomocysteinemia was reported in 28% of patients with peripheral artery disease, 42% of patients with cerebrovascular disease, and 30% of patients with CAD. The authors suggested that elevation of homocysteine level was an independent risk factor for vascular diseases. Therefore, hyperhomocysteinemia is accepted as an important marker due to its correlation with the aneurysms and other vascular diseases. Also, atherosclerosis has been shown to play a key role in the etiopathogenesis of aortic aneurysms.[8,9]

Hyperhomocysteinemia has been investigated in several studies for two decades and its relationship with aneurysms has been clearly demonstrated.[10,11] In the study by Brunelli et al.[10] including 58 patients undergoing AAA surgery, hyperhomocysteinemia was present in about half of the patients (48%). The authors also reported a significant correlation between AAA and hyperhomocysteinemia independent from other cardiovascular risk factors such as hypertension, smoking, and dyslipidemia. In addition, Warsi et al.[11] clearly showed this correlation between AAAs and homocysteine levels in their study including 74 AAA patients. Halazun et al.[12] conducted a study in 108 patients with AAAs and reported that increased homocysteine level was associated with an increased AAA diameter (>10 mm/year). In a large-scale study by Cao et al.[13] involving 463 AAA patients and 463 age- and sex-matched controls, homocysteine level, folic acid level, and MTFRC677T mutation were evaluated. Similarly, the aforementioned authors found a correlation between the increased homocysteine levels and the increased frequency of AAA. In another large-scale

study by Arnesen et al.,[14] serum total homocysteine level was found to be an independent risk factor for coronary heart disease with no threshold value. In the present study, consistent with the literature, homocysteine level in the AAA patients was also found to be significantly higher than that in the control group. On the other hand, when the patients with AAA were compared with the CAD patients who underwent CABG, homocysteine levels were also significantly higher in the AAA patients. However, there was no significant difference in the homocysteine levels between the CABG and control groups.

The main limitations of the present study include its single-center design with a small sample size.

In conclusion, our study results suggest that homocysteine level may be associated with AAA. Although CAD and AAA have the same atherosclerotic origin in the majority of cases, homocysteine levels may increase in patients with AAAs and, thus, may be useful to identify patients with an AAA.

Declaration of conflicting interests

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